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03/004488 A1

(54) Title: INDAZOLE BENZIMIDAZOLE COMPOUNDS AS TYROSINE AND SERINE/THREONINE KINASE INHIBITORS

(57) Abstract: Organic compounds having the structure I are provided where the variables have the values described herein. Pharmaceutical formulations and medicaments include the organic compound or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compound or a pharmaceutically acceptable salt of the organic compound with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation or medicament according to the invention to a patient in need thereof.

INDAZOLE BENZIMIDAZOLE COMPOUNDS AS TYROSINE AND SERINE/THREONINE KINASE INHIBITORS

FIELD OF THE INVENTION

This invention pertains generally to methods and compositions for treating a variety of patients and cell subjects. More particularly, the present invention provides novel compositions of matter and methods for angiogenesis inhibition, treating cancer, treating diabetes, stimulating insulin-dependent processes, treating Alzheimer's disease, treating central nervous system disorders, prolonging immune responses, reducing the splitting of centrosomes, blocking DNA repair, modulating cell cycle arrest, and inhibiting enzymes such as serine/threonine kinases and tyrosine kinases. The present invention thus has application in the areas of oncology, diabetes, immunology, and medicinal chemistry.

BACKGROUND OF THE INVENTION

Capillaries reach into almost all tissues of the human body and supply tissues with oxygen and nutrients as well as removing harmful waste products. Under typical conditions, the endothelial cells lining capillaries do not divide, and 15 capillaries, therefore, do not normally increase in number or size in a human adult. Under certain normal conditions, however, such as when a tissue is damaged, or during certain parts of the menstrual cycle, capillaries begin to proliferate rapidly. This process of forming new capillaries from pre-existing blood vessels is known as angiogenesis or neovascularization. See Folkman, J. Scientific American 275, 150-20 154 (1996). Angiogenesis during wound healing is an example of pathophysiological neovascularization during adult life. During wound healing, the additional capillaries provide a supply of oxygen and nutrients, promote granulation tissue, and aid in waste removal. After termination of the healing process, the capillaries normally regress. Lymboussaki, A. "Vascular Endothelial Growth 25 Factors and their Receptors in Embryos, Adults, and in Tumors" Academic

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Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999).

Angiogenesis also plays an important role in the growth of cancer cells. It is known that once a nest of cancer cells reaches a certain size, roughly 1 to 2 mm in diameter, the cancer cells must develop a blood supply in order for the tumor to grow larger as diffusion will not be sufficient to supply the cancer cells with enough oxygen and nutrients. A compound that inhibits angiogenesis will thus act to retard or halt the growth of cancer cells.

Receptor tyrosine kinases (RTKs) are polypeptides that regulate 10 developmental cell growth and differentiation and remodeling and regeneration of adult tissues. Mustonen, T. et al., J. Cell Biology 129, 895-898 (1995); van der Geer, P. et al. Ann Rev. Cell Biol. 10, 251-337 (1994). Polypeptide ligands known as growth factors or cytokines, are known to activate RTKs. Signaling involves ligand binding and a shift in conformation in the external domain of the receptor 15 resulting in its dimerization. Lymboussaki, A. "Vascular Endothelial Growth Factors and their Receptors in Embryos, Adults, and in Tumors" Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999); Ullrich, A. et al., Cell 61, 203-212 (1990). Binding of the ligand to the RTK results in receptor trans-20 phosphorylation at specific tyrosine residues and activation of the catalytic domains for the phosphorylation of cytoplasmic substrates. Id.

Two subfamilies of RTKs are specific to the vascular endothelium. These include the VEGF subfamily and the Tie receptor subfamily. Class III RTKs include VEGFR-1, VEGFR-2, and VEGFR-3. Shibuya, M. et al., Oncogene 5, 519-525 (1990); Terman, B. et al., Oncogene 6, 1677-1683 (1991); Aprelikova, O. et al., Cancer Res. 52, 746-748 (1992).

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A number of substances have been identified that promote angiogenesis. These include angiopoietin-1, basic fibroblast growth factor (bFGF)

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and vascular endothelial growth factor (VEGF). VEGF was first described as a protein able to induce vascular permeability and endothelial cell proliferation and was identified as a major inducer of angiogenesis and vasculogenesis. Ferrara, N. et al., Endocrinol. Rev. 18, 4-25 (1997). VEGF is known to specifically bind to RTKs including VEGFR-1 and VEGFR-2. DeVries, C. et al., Science 255, 989-991 (1992); Quinn, T. et al., Proc. Natl. Acad. Sci. 90, 7533-7537 (1993). It is now known that VEGF stimulates the migration and proliferation of endothelial cells and induces angiogenesis both in vitro and in vivo. Connolly, D. et al., J. Biol. Chem. 264, 20017-20024 (1989); Connolly, D. et al., J. Clin. Invest. 84, 1470-1478 (1989); Ferrara, N. et al., Endocrino. Rew. 18, 4-25 (1997); Leung, D. et al., Science 246, 1306-1309 (1989); Plouet, J. et al., EMBO J 8, 3801-3806 (1989).

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Because angiogenesis is known to be critical to the growth of cancer and to be controlled by VEGF and VEGF-RTK, substantial efforts have been undertaken to develop compounds which inhibit or retard angiogenesis and inhibit VEGF-RTK.

Platelet derived growth factor receptor kinase (PDGFRK) is another type of RTK. PDGF expression has been shown in a number of different solid tumors, from glioblastomas to prostate carcinomas. In these various tumor types, the biologicical role of PDGF signaling can vary from autocrine stimulation of cancer cell growth to more subtle paracrine interactions involving adjacent stroma and angiogenesis. Therefore, inhibiting the PDGFR kinase activity with small molecules may interfere with tumor growth and angiogenesis.

Tie-2 is a membrane RTK. Upon binding to its ligand, Tie-2 is activated and phosphorylates its downstream signal proteins. Tie-2 kinase activity may then trigger a pathway of cellular response that leads to stabilization of vascular vessels in cancer. Therefore, blocking kinase activity of Tie-2, in synergy with blockage of activity of other angiogenic kinases such as VEGF and bFGF receptor kinases, may be effective in cutting off the blood supply to cancer cells and in treating the disease.

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Glycogen synthase kinase 3 (GSK-3) is a serine/threonine kinase for which two isoforms, α and β, have been identified. Woodgett, *Trends Biochem*. *Sci.*, 16:177-81 (1991). Both GSK-3 isoforms are constitutively active in resting cells. GSK-3 was originally identified as a kinase that inhibits glycogen synthase by direct phosphorylation. Upon insulin activation, GSK-3 is inactivated, thereby allowing the activation of glycogen synthase and possibly other insulin-dependent events, such glucose transport. Subsequently, it has been shown that GSK-3 activity is also inactivated by other growth factors that, like insulin, signal through receptor tyrosine kinases (RTKs). Examples of such signaling molecules include IGF-1 and EGF. Saito et al., *Biochem. J.*, 303:27-31 (1994); Welsh et al., *Biochem. J.* 294:625-29 (1993); and Cross et al., *Biochem. J.*, 303:21-26 (1994).

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Agents that inhibit GSK-3 activity are useful in the treatment of disorders that are mediated by GSK-3 activity. In addition, inhibition of GSK-3 mimics the activation of growth factor signaling pathways and consequently GSK-3 inhibitors are useful in the treatment of diseases in which such pathways are insufficiently active. Examples of diseases that can be treated with GSK-3 inhibitors are described below.

Type 2 diabetes is an increasingly prevalent disease of aging. It is initially characterized by decreased sensitivity to insulin and a compensatory elevation in circulating insulin concentrations, the latter of which is required to maintain normal blood glucose levels. Increased insulin levels are caused by increased secretion from the pancreatic beta cells, and the resulting hyperinsulinemia is associated with cardiovascular complications of diabetes. As insulin resistance worsens, the demand on the pancreatic beta cells steadily increases until the pancreas can no longer provide adequate levels of insulin, resulting in elevated levels of glucose in the blood. Ultimately, overt hyperglycemia and hyperlipidemia occur, leading to the devastating long-term complications associated with diabetes, including cardiovascular disease, renal failure and blindness. The exact mechanism(s) causing type 2 diabetes are unknown, but result in impaired

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glucose transport into skeletal muscle and increased hepatic glucose production, in addition to inadequate insulin response. Dietary modifications are often ineffective, therefore the majority of patients ultimately require pharmaceutical intervention in an effort to prevent and/or slow the progression of the complications of the disease. Many patients can be treated with one or more of the many oral anti-diabetic agents available, including sulfonylureas, to increase insulin secretion. Examples of sulfonylurea drugs include metformin for suppression of hepatic glucose production, and troglitazone, an insulin-sensitizing medication. Despite the utility of these agents, 30-40% of diabetics are not adequately controlled using these medications and require subcutaneous insulin injections. Additionally, each of these therapies has associated side effects. For example, sulfonylureas can cause hypoglycemia and troglitazone can cause severe hepatoxicity. Presently, there is a need for new and improved drugs for the treatment of prediabetic and diabetic patients.

As described above, GSK-3 inhibition stimulates insulin-dependent 15 processes and is consequently useful in the treatment of type 2 diabetes. Recent data obtained using lithium salts provides evidence for this notion. The lithium ion has recently been reported to inhibit GSK-3 activity. Klein et al., PNAS 93:8455-9 (1996). Since 1924, lithium has been reported to have antidiabetic effects including the ability to reduce plasma glucose levels, increase glycogen uptake, potentiate 20 insulin, up-regulate glucose synthase activity and to stimulate glycogen synthesis in skin, muscle and fat cells. However, lithium has not been widely accepted for use in the inhibition of GSK-3 activity, possibly because of its documented effects on molecular targets other than GSK-3. The purine analog 5-iodotubercidin, also a GSK-3 inhibitor, likewise stimulates glycogen synthesis and antagonizes inactivation 25 of glycogen synthase by glucagon and vasopressin in rat liver cells. Fluckiger-Isler et al., Biochem J. 292:85-91 (1993); and Massillon et al., Biochem J. 299:123-8 (1994). However, this compound has also been shown to inhibit other serine/threonine and tyrosine kinases. Massillon et al., Biochem J. 299:123-8 (1994).

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GSK-3 is also involved in biological pathways relating to Alzheimer's disease (AD). The characteristic pathological features of AD are extracellular plaques of an abnormally processed form of the amyloid precursor protein (APP), so called β -amyloid peptide (β -AP) and the development of intracellular neurofibrillary tangles containing paired helical filaments (PHF) that consist largely of hyperphosphorylated tau protein. GSK-3 is one of a number of kinases that have been found to phosphorylate tau protein in vitro on the abnormal sites characteristic of PHF tau, and is the only kinase also demonstrated to do this in living cells and in animals. Lovestone et al., Current Biology 4:1077-86 (1994); and Brownlees et al., 10 Neuroreport 8: 3251-3255 (1997). Furthermore, the GSK-3 kinase inhibitor, LiCl, blocks tau hyperphosphorylation in cells. Stambolic et al., Current Biology 6:1664-8 (1996). Thus GSK-3 activity may contribute to the generation of neurofibrillary tangles and consequently to disease progression. Recently it has been shown that GSK-3β associates with another key protein in AD pathogenesis, presenillin 1 15 (PS1). Takashima et., PNAS 95:9637-9641 (1998). Mutations in the PS1 gene lead to increased production of β-AP, but the authors also demonstrate that the mutant PS1 proteins bind more tightly to GSK-3\beta and potentiate the phosphorylation of tau, which is bound to the same region of PS1.

It has also been shown that another GSK-3 substrate, β-catenin, binds
to PS1. Zhong et al., *Nature* 395:698-702 (1998). Cytosolic β-catenin is targeted for
degradation upon phosphorylation by GSK-3 and reduced β-catenin activity is
associated with increased sensitivity of neuronal cells to β-AP induced neuronal
apoptosis. Consequently, increased association of GSK-3β with mutant PS1 may
account for the reduced levels of β-catenin that have been observed in the brains of
PS1-mutant AD patients and to the disease related increase in neuronal cell-death.
Consistent with these observations, it has been shown that injection of GSK-3
antisense but not sense, blocks the pathological effects of β-AP on neurons in vitro,
resulting in a 24 hour delay in the onset of cell death and increased cell survival at 1
hr from 12 to 35%. Takashima et al., *PNAS* 90:7789-93. (1993). In these latter
studies, the effects on cell-death are preceded (within 3-6 hours of β-AP

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administration) by a doubling of intracellular GSK-3 activity, suggesting that in addition to genetic mechanisms that increase the proximity of GSK-3 to its substrates, β-AP may actually increase GSK-3 activity. Further evidence for a role for GSK-3 in AD is provided by the observation that the protein expression level (but, in this case, not specific activity) of GSK-3 is increased by 50% in postsynaptosomal supernatants of AD vs. normal brain tissue. Pei et al., *J. Neuropathol Exp.*, 56:70-78 (1997). Thus, specific inhibitors of GSK-3 should slow the progression of Alzheimer's Disease.

In addition to the effects of lithium described above, there is a long history of the use of lithium to treat bipolar disorder (manic depressive syndrome). This clinical response to lithium may reflect an involvement of GSK-3 activity in the etiology of bipolar disorder, in which case GSK-3 inhibitors could be relevant to that indication. In support of this notion it was recently shown that valproate, another drug commonly used in the treatment of bipolar disorder, is also a GSK-3 inhibitor. Chen et al., J. Neurochemistry, 72:1327-1330 (1999). One mechanism by which lithium and other GSK-3 inhibitors may act to treat bipolar disorder is to increase the survival of neurons subjected to aberrantly high levels of excitation induced by the neurotransmitter, glutamate. Nonaka et al., PNAS 95: 2642-2647 (1998). Glutamate-induced neuronal excitotoxicity is also believed to be a major cause of neurodegeneration associated with acute damage, such as in cerebral ischemia, traumatic brain injury and bacterial infection. Furthermore it is believed that excessive glutamate signaling is a factor in the chronic neuronal damage seen in diseases such as Alzheimer's, Huntingdon's, Parkinson's, AIDS associated dementia, amyotrophic lateral sclerosis (AML) and multiple sclerosis (MS). Thomas, J. Am. Geriatr. Soc. 43: 1279-89 (1995). Consequently, GSK-3 inhibitors should provide a useful treatment in these and other neurodegenerative disorders.

GSK-3 phosphorylates transcription factor NF-AT and promotes its export from the nucleus, in opposition to the effect of calcineurin. Beals et al., Science 275:1930-33 (1997). Thus, GSK-3 blocks early immune response gene

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activation via NF-AT, and GSK-3 inhibitors may tend to permit or prolong activation of immune responses. Thus, GSK-3 inhibitors are believed to prolong and potentiate the immunostimulatory effects of certain cytokines, and such an effect may enhance the potential of those cytokines for tumor immunotherapy or indeed for immunotherapy in general.

Lithium has other biological effects. It is a potent stimulator of hematopoiesis, both in vitro and in vivo. Hammond et al., *Blood* 55: 26-28 (1980). In dogs, lithium carbonate eliminated recurrent neutropenia and normalized other blood cell counts. Doukas et al. *Exp. Hematol*. 14: 215-221 (1986). If these effects of lithium are mediated through the inhibition of GSK-3, GSK-3 inhibitors may have even broader applications. Since inhibitors of GSK-3 are useful in the treatment of many diseases, the identification of new inhibitors of GSK-3 would be highly desirable.

NEK-2 is a mammalian serine threonine kinase, which is structurally related to the NimA kinase from the fungus Aspergillus nidulans. Mutations in NimA result in G2 phase arrest of cells and overexpression of wt NimA results in premature chromatin condensation, even when ectopically expressed in mammalian cells. Both protein and kinase levels peak in S/G2 phase of the cell cycle. NimA also appears to be required for the localization of cdk1/cyclinB complex to the nucleus and spindle pole body. Histone H3 has been shown to be an in vitro substrate for the kinase, and if this is also the case in vivo, it may explain the role of the kinase in chromosome condensation. Six NimA kinases have been identified to date in mammals, and of these, NEK-2 appears to be the most closely related to NimA. It's activity is also cell cycle regulated, peaking in S/G2 phase.

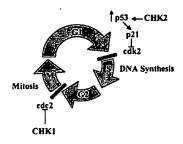
Overexpression of NEK-2, however, does not affect chromatin condensation but instead results in a pronounced splitting of centrosomes, possibly due to the loss of

centriole/centriole adhesion. There is evidence that NEK-2 is regulated by phosphorylation and can interact with protein phosphatase PP1. NEK-2 is

ubiquitously expressed and appears to be most abundant in testis. Hyseq cluster

374113, containing only NEK-2 sequences shows dramatic overexpression of NEK-2 in lymph node metastasis (13.3x) and in primary tumor (6.5x). Inhibition of NEK-2 by antisense oligonucleotides inhibited cell proliferation and reduced the capability of cells to grow in soft agar. In addition, increased cell death was observed in these cells both in the presence and absence of cisplatin.

Ultraviolet light, ionizing radiation, environmental agents and cytotoxic drugs can result in damage to cellular DNA integrity. When such damage occurs during DNA replication or cell division it is potentially catastrophic and may result in cell death. The cellular response is to arrest the cell cycle at one of two checkpoints (G1/S or G2/M) to either permit DNA repair or initiate apoptosis.



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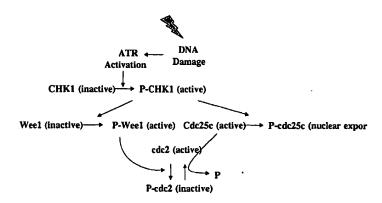
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The G1/S checkpoint is regulated by the p53 transcriptional activator protein and the absence of this critical protein is often an important step in tumorigenesis, thus defining p53 as a tumor suppressor. In fact, nearly 50% of all cancers are p53 defective due to mutation. T. Soussi, *Ann. N.Y. Acad Sci.*, 910, 121 (2001). In response to DNA damage, checkpoint kinase 2 (CHK-2) phosphorylates p53 and this results in stabilization of the protein and an elevation in p53 levels. A. Hirao et al., *Science*, 287, 1824 (2000). Consequently, negative cell cycle regulators, such as p21Waf1/Cip1, are activated and halt the cell cycle at the G1/S checkpoint. B. Vogelstein et al., *Nature*, 408, 307 (2000).

The G2/M checkpoint is monitored by the serine/threonine checkpoint kinase 1 (CHK-1). Upon DNA damage, the protein kinase ATR (ataxiatelangiectasia mutated - rad53 related kinase) is activated. H. Zhao et al., *Mol. Cell Biol.*, 21, 4129 (2001); Q. Liu et al., *Genes Dev.*, 14, 1448 (2000). SATR-

dependent phosphorylation of CHK-1 promotes its phosphorylation of cdc25 and Weel and ultimately inactivation of cdc 2. Thus, CHK-1 phosphorylation of cdc25c targets it for nuclear export to the cytoplasm and as a result the cdc25c phosphatase is rendered unavailable to activate cdc 2 by dephosphorylation. Y. Sanchez et al., 5 Science, 277, 1497 (1997); C. Y. Peng et al., Science, 277, 1501 (1997); T. A. Chen et al., Nature, 401, 616 (1999); and A. Lopez-Girona et al., Nature, 397, 172 (1999). In addition, CHK-1 activates the protein kinase Wee1, which phosphorylates and inactivates cdc 2. J. Lee et al. Mol. Biol. Cell, 12, 551 (2001); L. L. Parker et al., Science, 257, 1955 (1992). These dual pathways thus converge 10 to result in cell cycle arrest. Because cell cycle arrest is a potential mechanism by which tumor cells can overcome the damage induced by cytotoxic agents, abrogation of these checkpoints with novel therapeutic agents should increase the sensitivity of tumors to chemotherapy. The presence of two checkpoints, coupled with the tumor specific abrogation of one of these by p53 mutations in 50% of cancers, can be 15 exploited to design tumor-selective agents. Thus, in p53 minus tumors, therapeutic inhibition of G2/M arrest leaves cancerous cells no options for DNA damage repair and results in apoptosis. Normal cells have wild type p53 and retain an intact G1/S checkpoint. Thus these cells have an opportunity to correct DNA damage and survive. One approach to the design of chemosensitizers that abrogate the G2/M 20 checkpoint is to identify inhibitors of the key G2/M regulatory kinase, CHK-1.



The synthesis of various quinoline derivatives is disclosed in WO 97/48694. These compounds are disclosed as capable of binding to nuclear

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hormone receptors and being useful for stimulating osteoblast proliferation and bone growth. The compounds are also disclosed as being useful in the treatment or prevention of diseases associated with nuclear hormone receptor families.

Various quinoline derivatives in which the benzene ring of the quinolone is substituted with a sulfur group are disclosed in WO 92/18483. These compounds are disclosed as being useful in pharmaceutical formulations and as medicaments.

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Various indolyl substituted compounds have recently been disclosed in WO 01/29025, and various benzimidazolyl substituted compounds have recently been disclosed in WO 01/28993. Such compounds are reportedly capable of inhibiting, modulating and/or regulating signal transduction of both receptor-type and non-receptor type tyrosine kinases. Neither of the PCT publications discloses benzimidazole-substituted indazoles.

Various indazole compounds and pharmaceutical formulations containing them are disclosed in WO 01/02369 and recently published WO 01/53268. Such compositions are purportedly useful for mediating tyrosine kinase signal transduction and thereby modulating and/or inhibiting cell proliferation. Some of the disclosed compounds include the benzimidazole group. Various benzimidazoles substituted with -C(=O)-NH₂ are disclosed in WO 00/68206 as useful as inhibitors of the enzyme poly(ADP-ribose)polymerase and for use in producing medicaments.

A continuing need exists for compounds that inhibit the proliferation of capillaries, inhibit the growth of tumors, treat cancer, treat diabetes, stimulate insulin-dependent processes, treat Alzheimer's disease, treat central nervous system disorders, prolong immune responses, reduce the splitting of centrosomes, block DNA repair, modulate cell cycle arrest, and/or inhibit enzymes such as flt-1 (VEGFR2), KDR (VEGFR2), Flk-1, bFGFR, GSK-3, NEK-2, CHK-1, Tie-2, PDGF, and cdc 2, and pharmaceutical formulations and medicaments that contain

such compounds. A need also exists for methods for administering such compounds, pharmaceutical formulations, and medicaments to patients or subjects in need thereof.

SUMMARY OF THE INVENTION

The present invention provides compounds, pharmaceutical formulations and medicaments including the compounds, methods of preparing the pharmaceutical formulations, medicaments, and compounds, and methods of treating patients with the pharmaceutical formulations and compounds.

The present invention provides compounds having the structure I.

The invention also provides tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure I has the following formula:

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$$R^{5} \qquad Z^{1} \qquad Z^{2} \qquad Z^{3} \qquad R^{7} \qquad R^{8} \qquad R^{10} \qquad R^{10} \qquad R^{2} \qquad R^{3} \qquad R^{4} \qquad R^{8} \qquad R^{9} \qquad R^{10} \qquad R^{$$

where, in a first group of compounds:

I

 Z^1 , Z^2 , Z^3 , and Z^4 are selected independently from C or N;

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R¹-R⁸ are selected independently from the group consisting of -H, -F, -Cl, -Br, -C≡N, -NO₂, -CF₃, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, 5 substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted alkylheterocyclyl groups, substituted and unsubstituted 10 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heteroaryl groups, substituted and unsubstituted -C(=0)-N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl 15 groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=0)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heteroaryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups. substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-20 alkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted heteroaryl groups, and substituted and unsubstituted heterocyclyl groups;

$$R^9$$
 is -H, -C(=O)-alkyl, or -C(=O)-aryl; and

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$$R^{10}$$
 is -H, -C(=O)-alkyl, or -C(=O)-aryl.

More particular embodiments of the compounds of the invention having the general structure shown in I above are provided in a second group of compounds. The second group of compounds are those for which:

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Z¹, Z², Z³, and Z⁴ are independently selected from C or N;

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R¹ is selected from -H, -F, -Cl, and -Br;

R² is selected from -H, -F, -Cl, -Br, -C≡N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=0)O-alkyl groups, substituted and unsubstituted -5 C(=0)O-aryl groups, substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, 10 substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, and 15 substituted and unsubstituted heterocyclylalkoxy groups;

R³ is selected from -H, -F, -Cl, -Br, and substituted and unsubstituted alkoxy groups;

 R^4 is -H;

R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy

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groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, and substituted and unsubstituted -C(=O)N(H)heterocyclyl groups; or R⁶ is absent if Z² is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and 15 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl 20 groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, and substituted and unsubstituted -C(=O)N(H)heterocyclyl groups; or R⁷ is absent if Z³ is N;

 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R9 is -H: and

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 R^{10} is -H. In some embodiments of the second group of compounds, at least one of R^1 , R^2 , R^3 , R^5 , R^6 , R^7 or R^8 is not -H. In other such embodiments, at least two of R^1 , R^2 , R^3 , R^5 , R^6 , R^7 or R^8 are not -H.

In some embodiments of the second group of compounds, R³ is selected from -F, -Cl, -Br, and substituted and unsubstituted alkoxy groups.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a third group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

R¹ is selected from -H, -F, -Cl, -Br, -NO2, -C≡N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO2-alkyl groups, substituted and unsubstituted -N(H)-SO2-aryl groups, -N(H)-SO2-CF3 groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted and unsubstituted alkoxy groups, substituted and unsubstituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-

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heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-arvl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl 10 groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl groups, substituted and 15 unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

R² is selected from -H, -F, -Cl, -Br, -C≡N, -NO₂, -CO₂H, -OH,

substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino
groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups,
substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and
unsubstituted -C(=O)-N(H)-alkyl groups, and substituted and unsubstituted

-C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
-C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl
groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and
unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups,
substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and

unsubstituted -N(H)C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups. substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and 10 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 15 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 20 unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-25 C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂Osuch that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms;

R³ is selected from -H, -F, -Cl, -Br, -CF₃, -C≡N, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)-O-alkyl groups,

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substituted and unsubstituted amino groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted saturated heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl 10 groups, substituted and unsubstituted -N(H)C(=0)N(H)-aryl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 15 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl 20 groups;

R⁴ is -H, -F, -Br, -Cl, -NO₂, -C≡N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted

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and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 5 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl 10 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl 15 groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-20 C(=O)-alkyl-heterocyclyl groups;

R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy

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groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted aryloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

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R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

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-C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N;

 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R9 is -H; and

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R¹⁰ is selected from the group consisting of -H, and substituted or unsubstituted alkyl groups. In some such embodiments of the third group of compounds, at least one of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ is not -H. In other such embodiments, at least two of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ are not -H.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from -H, -F, -Cl, and -OMe.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C \equiv N, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(\equiv O)N(H)-aryl groups; or R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)CH₂CH₃ group,

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a substituted or unsubstituted $-N(H)C(=O)N(H)CH(CH_3)_2$ group, a substituted or unsubstituted $-N(H)C(=O)N(H)C(CH_3)_3$ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group, a -N(H)C(=O)N(H)-(trifluoromethylphenyl) group, or the like.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -F, -C1, or - OMe.

In some embodiments of the third group of compounds, Z^1-Z^4 , R^1 , 10 and R² have any of the values in previous embodiments, and if R³ is H, at least one of R⁶ or R⁷ is selected from the group consisting of -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 15 arylheterocyclyl groups, substituted and unsubstituted cycloalkylheterocyclyl groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted -N(H)-alkyl groups, substituted and unsubstituted -N(H)-alkylheterocyclyl groups, substituted and unsubstituted -N(H)-alkyl-aryl groups, 20 substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups. In some such embodiments, if R³ is H, at least one of R⁶ or R⁷ is selected from the group consisting of -CO₂H, substituted and unsubstituted saturated heterocyclyloxy groups, 25 substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)heterocyclyl groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups.

In another embodiment of the third group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from a first group of compounds; or Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z3 is C, and R7 is selected from the first group of compounds, the first group of compounds comprising members selected from the group consisting of -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl 10 groups, substituted and unsubstituted cycloalkylheterocyclyl groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and 15 unsubstituted -C(=O)N(H)-aryl groups, -C(=O)N(H)-heteroaryl groups, substituted and unsubstituted -C(=O)N(alkyl) (heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups.

In another embodiment of the third group of compounds, Z^1 , Z^3 , Z^4 . R¹, R², R³, R⁵, and R⁸ have any of the values defined in the previous embodiments, Z² is C, and R⁶ is a substituted or unsubstituted heterocyclyl group. In some 20 embodiments of the third group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted 25 and unsubstituted piperidinyl groups, substituted and unsubstituted pyrazolyl groups, substituted and unsubstituted pyrrolyl groups substituted and unsubstituted imidazolyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2,5-diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4-diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 30

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1.4-diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4-diazacycloheptane groups. In still other embodiments of the third group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, 5 but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but 10 not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl 15 substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, 20 but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl 25 substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=O)O-alkyl substituted piperazinyl group; a -C(=0)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=O)-ethyl or a -C(=O)-methyl substituted piperazinyl 30

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group, and the like such as a piperazinyl group where the -C(=0)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z^2 , and the like: a - C(=0)O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to \mathbb{Z}^2 , and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4-hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as, but not limited to, a dialkylamino substituted pyrrolidinyl group such as,

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but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2.5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2,5diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the third group of compounds where R⁶ is a substituted or unsubstituted heterocyclyl group, R⁷ is -H.

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In another embodiment of the third group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the third group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted pyrrolyl groups, substituted pyrazolyl groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 2,5-

diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1,4diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4diazacycloheptane groups. In still other embodiments of the third group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is an 5 unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an 10 aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl 15 group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted 20 piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted 25 piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl 30

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substituted piperazinyl group; a -C(=0)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=O)-ethyl or a -C(=O)-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z^3 , and the like; a -C(=O)O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted

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pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as. but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N, N-dimethylamino substituted 5 pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy 10 substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5-diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2,5-diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or 15 unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4-diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4-diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In 20 still other embodiments of the third group of compounds where R⁷ is a substituted or unsubstituted heterocyclyl group, R⁶ is -H.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a fourth group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

R¹ is selected from -H, -F, -Cl, -Br, -NO₂, -C≡N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted and unsubstituted and

unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted $-N(H)-SO_2$ -alkyl groups, substituted and unsubstituted $-N(H)-SO_2$ -aryl groups, $-N(H)-SO_2-CF_3$ groups, substituted and unsubstituted

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- -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, and substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 15 C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted

-alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-

- 20 heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-
- 25 C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

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 R^2 is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(\equiv O)O-alkyl groups, substituted and unsubstituted -C(\equiv O)O-aryl groups,

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substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and 5 unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, 10 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and 15 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 20 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl 25 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups. 30

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substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-

C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂O-such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms;

R³ is selected from -H, -F, -Cl, -Br, -CF₃, -C≡N, -NO₂, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl 10 groups, substituted and unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted 15 -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted 20 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 25 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-arvl groups, and substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl 30 groups;

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C(=O)-alkyl-heterocyclyl groups;

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 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=0)-O-alkyl groups, -OH. substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted 5 aryloxy groups, substituted and unsubstituted -N(H)-C(=0)-aryl groups, substituted and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and 10 unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 15 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-20 heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl 25 groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-

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 R^5 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^5 is absent if Z^1 is N;

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R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁶ is absent if Z² is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted

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arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted and unsubstituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R⁷ is absent if Z³ is N;

 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R⁹ is -H: and

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R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups. In some such embodiments of the fourth group of compounds, at least one of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ is not -H. In other such embodiments, at least two of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ are not -H.

In some embodiments of the fourth group of compounds, R¹ is an unsubstituted -NH₂ group or is a substituted or unsubstituted heterocyclylamino group such as, but not limited to, substituted and unsubstituted pyrroldinylalkylamino groups and the like, such as, but not limited to, substituted and unsubstituted pyrroldinylmethylamino groups and the like such as, but not limited to, -N(H)-CH₂-(2-pyrroldinyl) groups and the like.

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In another embodiment of the fourth group of compounds, R² is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and unsubstituted pyrrolidinylalkylamino groups, and substituted and unsubstituted aminoalkylamino groups. In other such embodiments, R² is selected from the group consisting of -N(H)-CH₂-(2-thiazolyl) groups, -N(H)-CH₂-(2-pyrroldinyl groups), -N(H)-CH₂-CH₂-N(H)(alkyl) groups, and -NH-CH₂CH₂-N(alkyl)₂ groups. In still other such embodiments, R² is selected from the group consisting of -N(H)-CH₂-(2-thiazolyl) groups, -N(H)-CH₂-(2-pyrroldinyl groups), -N(H)-CH₂-(2-thiazolyl) groups, and -NH-CH₂-CH₂-N(CH₃)₂ groups.

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In another embodiment of the fourth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-aryl groups and substituted and unsubstituted -C(\equiv O)N(H)-alkyl-heterocyclyl groups; or R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the fourth group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups. In some such embodiments, R^3 is a substituted or unsubstituted $-N(H)C(=O)N(H)CH_2CH_3$ group, a substituted or unsubstituted $-N(H)C(=O)N(H)CH(CH_3)_2$ group, a substituted or unsubstituted $-N(H)C(=O)N(H)C(CH_3)_3$ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited

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to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group, a-N(H)C(=O)N(H)-(trifluoromethylphenyl) group, or the like.

In other embodiments of the fourth group of compounds, R³ is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and unsubstituted benzimidazolylalkylamino groups, substituted and unsubstituted imidazolylalkylamino groups, substituted and unsubstituted furanylalkylamino groups, and substituted and unsubstituted arylalkylamino groups. In some such embodiments, R³ is selected from the group consisting of (2-thiazolyl)alkylamino groups, 1-(3-methylbenzimidazolyl)alkylamino 10 groups, 4-(2-phenylimidazolyl)alkylamino groups, 4-(2-ethyl-5-methylimidazolyl)alkylamino groups, (2-furanyl)alkylamino groups, phenylalkylamino groups, and 1-(2-fluoro-5-alkoxyphenyl)alkylamino groups. In still other such embodiments, R³ is selected from the group consisting of -N(H)-CH₂-(2-thiazolyl) groups, -N(H)-CH₂-(1-(3-methylbenzimidazolyl)) groups, -N(H)-CH₂-(4-(2-phenylimidazolyl)) groups, -N(H)-CH₂-(4-(2-ethyl-5-15 methylimidazolyl)) groups, -N(H)-CH₂-(2-furanyl) groups, -N(H)-CH₂-phenyl groups, and -N(H)-CH₂-(1-(2-fluoro-5-alkoxyphenyl)) groups.

In still another embodiment, R¹ is selected from the group consisting of unsubstituted -NH₂ groups, and substituted and unsubstituted

20 pyrrolidinylalkylamino groups; R² is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and unsubstituted aminoalkylamino groups; and/or R³ is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and

25 unsubstituted benzimidazolylalkylamino groups, substituted and unsubstituted imidazolylalkylamino groups, substituted and unsubstituted imidazolylalkylamino groups, substituted and unsubstituted furanylalkylamino groups, and substituted and unsubstituted arylalkylamino groups. In such compounds, Z¹-Z⁴, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, and R¹⁰ can have any of the other values described in any of the other embodiments of any of the groups of compounds.

In another embodiment of the fourth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from a first group; or Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from the first group, the first group comprising members selected from the group consisting of -Br. -5 CO2H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted 10 cycloalkylheterocyclyl groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and 15 unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups. In some such embodiments, R³ is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C=N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and 20 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, and substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups; or R^2 and R^3 are a group of formula -OCH2O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a fifth group of compounds for which:

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 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

R¹ is selected from -H, -F, -Cl, -Br, -NO₂, -C≡N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and

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unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=0)-arvl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 5 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, and substituted and unsubstituted -C(=O)-N(H)-alkyl-10 heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 15 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl 20 groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and 25 unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl-heterocyclyl groups;

R² is selected from -H, -F, -Cl, -Br, -C≡N, -NO₂, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino

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groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups substituted and unsubstituted -C(=O)N(H)-5 aryl groups, substituted and unsubstituted -C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, 10 substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and 15 unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and 20 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted 30

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heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R^2 and R^3 are a group of formula -OCH₂O-such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms:

R³ is selected from -F, -Cl, -Br, -CF₃, -C≡N, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted saturated heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups;

R⁴ is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted -N(H)-SO₂-aryl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted

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and unsubstituted alkoxy groups substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 5 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-arvl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl 10 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl 15 groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-20 C(=O)-alkyl-heterocyclyl groups;

R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy

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groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R⁶ is absent if Z² is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

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-C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N;

 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R9 is -H; and

 $m R^{10}$ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a sixth group of compounds for which:

Z¹, Z², Z³, and Z⁴ are independently selected from C or N;

15 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl 20 groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted 25 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups.

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substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 5 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 10 unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-15 C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

R² is selected from -F, -Cl, -Br, -C≡N, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, substituted and 20 unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups. substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=0)-alkyl groups, substituted and unsubstituted 25 -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted $-N(H)-(SO_2)$ alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl 30

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groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms;

 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C=N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=0)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted 10 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, 15 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)NH-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl-20 heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted 30

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heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

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 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, 10 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl 15 groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups. substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and 20 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-25 C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted 30

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heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

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 R^5 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^5 is absent if Z^1 is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups. substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

-C(=0)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N;

R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

R⁹ is -H; and

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R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a seventh group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

5 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl 10 groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 15 groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 20 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl 25 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups.

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substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

5 C(=O)-alkyl-heterocyclyl groups;

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 R^2 is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=0)O-alkyl groups, substituted and unsubstituted -C(=0)O-aryl groups. 10 substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-arvl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and 15 unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, 20 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and 25 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 30

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(alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-arvl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl 5 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and 10 unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂Osuch that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms; 15

 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C=N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl 20 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted 25 -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, 30

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substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 5 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 10 unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted 15 -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, 20 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, 25 -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, 30 substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and

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unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 5 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 10 unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted 15 -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted and unsubstituted arylheterocyclyl groups, substituted alkylheterocyclyl groups, and

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substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R⁶ is absent if Z² is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and 15 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 20 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted 25 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups. substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁷ is absent if Z³ is N;

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R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

R⁹ is -H;

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 R^{10} is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups; and

at least one of Z² or Z³ is C and at least one of R⁶ or R⁷ is selected 10 from the group consisting of substituted and unsubstituted piperidinyl substituted heterocyclyl groups, substituted and unsubstituted heterocyclyl substituted piperidinyl groups, substituted and unsubstituted hydroxymethyl substituted piperidinyl groups, dimethylaminoalkyl substituted pyrrolidinyl groups, substituted and unsubstituted 3-alkyl substituted piperazinyl groups, substituted and 15 unsubstituted 3,5-dialkyl substituted piperazinyl groups, substituted and unsubstituted N-hydroxyalkyl substituted piperazinyl groups, substituted and unsubstituted 1,4-diazacycloheptyl groups, substituted and unsubstituted 1-aza-4oxacycloheptyl groups, substituted and unsubstituted N-ethylpiperazinyl groups, substituted and unsubstituted N-isopropylpiperazinyl groups, substituted and unsubstituted N-sec-butylpiperazinyl groups, substituted and unsubstituted N-2-20 pyridyl substituted piperazinyl groups, substituted and unsubstituted N-3-pyridyl substituted piperazinyl groups, substituted and unsubstituted N-4-pyridyl substituted piperazinyl groups, substituted and unsubstituted N(H)-CH2-pyridyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted 3-25 alkyl substituted morpholinyl groups, substituted and unsubstituted 3,5-dialkyl substituted morpholinyl groups, dialkylamino substituted pyrrolidinyl groups, pyrrolidinyl groups substituted with both dialkylamino and alkyl groups, substituted and unsubstituted 4-hydroxy substituted piperidinyl groups, substituted and unsubstituted 4-aryl substituted piperidinyl groups, substituted and unsubstituted 4-

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hydroxy-4-phenyl substituted piperidinyl groups, substituted and unsubstituted cyclohexylpiperazinyl groups, substituted and unsubstituted cyclopentylpiperazinyl groups, substituted and unsubstituted N-alkyl substituted diazabicycloalkane groups. substituted and unsubstituted -N(CH₃)(N-alkyl(4-piperidinyl)) groups, substituted 5 and unsubstituted piperazinyl groups further substituted with a -C(=O)-alkyl group on one of the N atoms of the piperazinyl group, substituted and unsubstituted -N(H)CH2CH2-imidazolyl groups, substituted and unsubstituted -N(H)CH2CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2CH2-morpholinyl groups, substituted and unsubstituted 10 -N(H)CH2CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH2CH2-pyridyl groups, substituted and unsubstituted -N(H)CH2CH2imidazolyl groups, substituted and unsubstituted -N(H)CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH₂CH₂-morpholinyl groups, substituted and 15 unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH₂CH₂-piperidinyl groups, substituted and unsubstituted -N(H)CH₂CH₂pyridyl groups, substituted and unsubstituted cyclobutylpiperazinyl groups, substituted and unsubstituted -OCH2-pyrrolidinyl groups, substituted and unsubstituted -OCH2CH2-pyrrolidinyl groups, substituted and unsubstituted 20 -OCH2CH2CH2-pyrrolidinyl groups, substituted and unsubstituted piperazinyl groups further substituted with a -CH₂C(=0)-O-alkyl group bonded to one of the N atoms of the piperazinyl group, substituted and unsubstituted piperazinyl groups further substituted with a -C(=O)-O-alkyl group bonded to one of the N atoms of the piperazinyl group, substituted and unsubstituted hydroxypyrrolidinyl groups, 25 substituted and unsubstituted hydroxypiperidinyl groups, substituted and unsubstituted -OCH₂-pyridyl groups, substituted and unsubstituted piperidinylamino groups, substituted and unsubstituted pyridyloxy groups with a -C(=O)-N(H)(alkyl)group bonded to a carbon atom of the pyridine ring of the pyridyloxy group, and substituted and unsubstituted pyridyloxy groups with a -C(=0)-N(alkyl)₂ group 30 bonded to a carbon atom of the pyridine ring of the pyridyloxy group.

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The invention further provides many other embodiments of compounds having the formula I and embodiments of the first, second, third, fourth, fifth, sixth, and seventh groups of compounds having the formula I.

Pharmaceutical formulations according to the present invention are provided which include any of the compounds described above in combination with a pharmaceutically acceptable carrier.

The invention further provides methods for synthesizing the compounds of formula I according to the first through seventh groups.

A method of treating a patient is also provided which includes

administering an effective amount of the pharmaceutical formulation according to
the present invention to a patient in need thereof.

A method for inhibiting tumor growth in a patient is provided and includes administering an effective amount of a compound according to the invention to a patient having a tumor.

A method for inhibiting the proliferation of capillaries in a patient in need is still further provided and includes administering an effective amount of a compound according to the present invention to a patient in need.

Various other methods for inhibiting enzymes and treating patients and cells are further disclosed in the following detailed description.

Further objects, features and advantages of the invention will be apparent from the following detailed description.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a novel class of compounds which act as inhibitors of receptor tyrosine kinases, including inhibitors of bFGF, VEGF-RTK, KDR, Flk-1, GSK-3, NEK-2, CHK-1, Tie-2, PDGF, and cdc 2. These

compounds can be formulated into pharmaceutical formulations that are useful in treating patients with a need for such inhibitors (e.g., those suffering from cancer). The compounds described herein are also useful for reducing capillary proliferation and in the treatment of cancer and other medical or cellular conditions in human and cell subjects.

The following abbreviations and definitions are used throughout this application:

. "VEGF" is an abbreviation that stands for vascular endothelial growth factor.

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10 "RTK" is an abbreviation that stands for receptor tyrosine kinase.

"VEGF-RTK" is an abbreviation that stands for vascular endothelial growth factor receptor tyrosine kinase.

"Flt-1" is an abbreviation that stands for fms-like tyrosine kinase-1, also known as vascular endothelial growth factor receptor-1 or VEGFR1.

15 "KDR" is an abbreviation that stands for kinase-insert domain tyrosine kinase, also known as vascular endothelial growth factor receptor-2 or VEGFR2.

"bFGF" is an abbreviation that stands for basic fibroblast growth factor.

20 "bFGFR" is an abbreviation that stands for basic fibroblast growth factor receptor.

"GSK-3" is an abbreviation that stands for glycogen synthase kinase 3.

"NEK-2" is an abbreviation that stands for NIM-A related kinase.

- "NIM-A" is an abbreviation that stands for never in mitosis.
- "CHK 1" is an abbreviation that stands for checkpoint kinase 1.
- "Cdc 2" is an abbreviation that stands for cell division cycle 2.
- "Tie-2" is an abbreviation that stands for tyrosine kinase with Ig and 5 EGF homology domains.
 - "PDGF" is an abbreviation that stands for platelet derived growth factor.
 - "Flk-1" is an abbreviation that stands for fetal liver tyrosine kinase 1.
 - "AD" is an abbreviation that stands for Alzheimer Disease.
- "APP" is an abbreviation that stands for amyloid precursor protein.
 - "PHF" is an abbreviation that stands for paired helical filaments.
 - "PS 1" is an abbreviation that stands for presentllin 1.
 - "MS" is an abbreviation that stands for multiple sclerosis.
 - "AML" is an abbreviation that stands for amyotropic lateral

15 sclerosis.

Generally, reference to a certain element such as hydrogen or H is meant to include all isotopes of that element. For example, if an R group is defined to include hydrogen or H, it also includes deuterium and tritium.

The phrase "unsubstituted alkyl" refers to alkyl groups that do not contain heteroatoms. Thus the phrase includes straight chain alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl and the like. The phrase also includes branched chain isomers of straight chain alkyl groups, including but not limited to, the following which are provided

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by way of example: $-CH(CH_3)_2$,

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CH(CH₃)₂.

-CH(CH₃)(CH₂CH₃), -CH(CH₂CH₃)₂, -C(CH₃)₃, -C(CH₂CH₃)₃,

-CH₂CH(CH₃)₂, -CH₂CH(CH₃)(CH₂CH₃), -CH₂CH(CH₂CH₃)₂, -CH₂C(CH₃)₃, -

CH₂C(CH₂CH₃)₃, -CH(CH₃)CH(CH₃)(CH₂CH₃), -CH₂CH₂CH(CH₃)₂,

5 -CH₂CH₂CH(CH₃)(CH₂CH₃), -CH₂CH₂CH(CH₂CH₃)₂, -CH₂CH₂C(CH₃)₃,

-CH₂CH₂C(CH₂CH₃)₃, -CH(CH₃)CH₂CH(CH₃)₂,

-CH(CH₃)CH(CH₃)CH(CH₃)₂, -CH(CH₂CH₃)CH(CH₃)CH(CH₃)(CH₂CH₃), and others. The phrase also includes cyclic alkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl and such rings substituted with straight and branched chain alkyl groups as defined above. Thus the phrase unsubstituted alkyl groups includes primary alkyl groups, secondary alkyl groups, and tertiary alkyl groups. Unsubstituted alkyl groups may be bonded to one or more carbon atom(s), oxygen atom(s), and/or nitrogen atom(s) in the parent compound. Preferred unsubstituted alkyl groups include straight and branched chain alkyl groups and cyclic alkyl groups having 1 to 20 carbon atoms. More preferred such unsubstituted alkyl groups have from 1 to 10 carbon atoms while even more preferred such groups have from 1 to 8, from 1 to 6 or from 1 to 4 carbon atoms. Other preferred unsubstituted alkyl groups include straight and branched chain alkyl groups having from 1 to 3 carbon atoms and include methyl, ethyl, propyl, and –

The phrase "substituted alkyl" refers to an unsubstituted alkyl group as defined above in which one or more bonds to a carbon(s) or hydrogen(s) are replaced by a bond to non-hydrogen and non-carbon atoms such as, but not limited to, a halogen atom such as F, Cl, Br, and I; an oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, and ester groups; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfone groups, sulfonyl groups, and sulfoxide groups; a nitrogen atom in groups such as amines, amides, alkylamines, dialkylamines, arylamines, alkylarylamines, diarylamines, N-oxides, imides, and enamines; a silicon atom in groups such as in trialkylsilyl groups, dialkylarylsilyl groups, alkyldiarylsilyl groups, and triarylsilyl groups; and other

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heteroatoms in various other groups. Substituted alkyl groups also include groups in which one or more bonds to a carbon(s) or hydrogen(s) atom is replaced by a higher-order bond (e.g., a double- or triple-bond) to a heteroatom such as oxygen in oxo, carbonyl, carboxyl, and ester groups; nitrogen in groups such as imines, 5 oximes, hydrazones, and nitriles. Substituted alkyl groups further include alkyl groups in which one or more bonds to a carbon(s) or hydrogen(s) atoms is replaced by a bond to an aryl, heterocyclyl group, or cycloalkyl group. Preferred substituted alkyl groups include, among others, alkyl groups in which one or more bonds to a carbon or hydrogen atom is/are replaced by one or more bonds to fluorine atoms. 10 Another preferred substituted alkyl group is the trifluoromethyl group and other alkyl groups that contain the trifluoromethyl group. Other preferred substituted alkyl groups include those in which one or more bonds to a carbon or hydrogen atom is replaced by a bond to an oxygen atom such that the substituted alkyl group contains a hydroxyl, alkoxy, or aryloxy group. Still other preferred substituted 15 alkyl groups include alkyl groups that have an amine, or a substituted or unsubstituted alkylamine, dialkylamine, arylamine, (alkyl)(aryl)amine, diarylamine, heterocyclylamine, diheterocyclylamine, (alkyl)(heterocyclyl)amine, or (aryl)(heterocyclyl)amine group.

The phrase "unsubstituted aryl" refers to aryl groups that do not

20 contain heteroatoms. Thus the phrase includes, but is not limited to, groups such as
phenyl, biphenyl, anthracenyl, naphthenyl by way of example. Although the phrase
"unsubstituted aryl" includes groups containing condensed rings such as
naphthalene, it does not include aryl groups that have other groups such as alkyl or
halo groups bonded to one of the ring members as aryl groups such as tolyl are

25 substituted aryl groups. A preferred unsubstituted aryl group is phenyl.

Unsubstituted aryl groups may be bonded to one or more carbon atom(s), oxygen
atom(s), and/or nitrogen atom(s) in the parent compound.

The phrase "substituted aryl group" has the same meaning with respect to unsubstituted aryl groups that substituted alkyl groups had with respect to

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unsubstituted alkyl groups. A substituted aryl group includes aryl groups in which one of the aromatic carbons is bonded to a non-carbon or non-hydrogen atom and also includes aryl groups in which one or more aromatic carbons of the aryl group is bonded to a substituted and/or unsubstituted alkyl group. Thus, the phrase "substituted aryl" includes, but is not limited to tolyl, and hydroxyphenyl among others.

The phrase "unsubstituted arylalkyl" refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to an aryl group as defined above. For example, methyl (-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a phenyl group, such as if the carbon of the methyl were bonded to a carbon of benzene, then the compound is an unsubstituted arylalkyl group. Thus the phrase includes, but is not limited to, groups such as benzyl, diphenylmethyl,

-CH(C_6H_5)(CH₃), and -CH₂CH₂(C_6H_5) among others.

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The phrase "substituted arylalkyl" has the same meaning with respect to unsubstituted arylalkyl groups that substituted aryl groups had with respect to unsubstituted aryl groups. However, a substituted arylalkyl group also includes groups in which a carbon or hydrogen bond of the alkyl part of the group is replaced by a bond to a non-carbon or a non-hydrogen atom. Examples of substituted arylalkyl groups include, but are not limited to, -CH₂C(=O)(C₆H₅), and -CH₂(2-methylphenyl) among others.

The phrase "unsubstituted heterocyclyl" refers to both aromatic and nonaromatic ring compounds containing 3 or more ring members of which one or more is a heteroatom such as, but not limited to, N, O, and S. Although the phrase "unsubstituted heterocyclyl" includes condensed heterocyclic rings such as benzimidazolyl and indazolyl, it does not include heterocyclyl groups that have other groups such as alkyl or halo groups bonded to one of the ring members because compounds such as 2-methylbenzimidazolyl are substituted heterocyclyl groups.

Examples of heterocyclyl groups include, but are not limited to: unsaturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1.2.3-triazolyl etc.), tetrazolyl, (e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl; condensed unsaturated heterocyclic groups containing 1 to 4 nitrogen atoms such as, but not limited to, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl; unsaturated 3 to 8 membered rings containing 1 to 2 10 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, oxazolyl, isoxazolyl, oxadiazolyl (e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5oxadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, morpholinyl; unsaturated condensed heterocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen 15 atoms, for example, benzoxazolyl, benzoxadiazolyl, benzoxazinyl (e.g. 2H-1,4benzoxazinyl etc.); unsaturated 3 to 8 membered rings containing 1 to 3 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolyl, isothiazolyl, thiadiazolyl (e.g. 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5thiadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 sulfur atoms 20 and 1 to 3 nitrogen atoms such as, but not limited to, thiazolodinyl; saturated and unsaturated 3 to 8 membered rings containing 1 to 2 sulfur atoms such as, but not limited to, thienyl, dihydrodithiinyl, dihydrodithionyl, tetrahydrothiophene, tetrahydrothiopyran; unsaturated condensed heterocyclic rings containing 1 to 2 25 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, benzothiazolyl, benzothiadiazolyl, benzothiazinyl (e.g. 2H-1,4-benzothiazinyl, etc.), dihydrobenzothiazinyl (e.g. 2H-3,4-dihydrobenzothiazinyl, etc.), unsaturated 3 to 8 membered rings containing oxygen atoms such as, but not limited to furanyl (the furan group); unsaturated condensed heterocyclic rings containing 1 to 2 oxygen atoms such as benzodioxolyl (e.g. 1,3-benzodioxoyl, etc.); unsaturated 3 to 8 30

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membered rings containing an oxygen atom and 1 to 2 sulfur atoms such as, but not limited to, dihydrooxathiinyl; saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 2 sulfur atoms such as 1,4-oxathiane; unsaturated condensed rings containing 1 to 2 sulfur atoms such as benzothienyl, benzodithiinyl; and unsaturated condensed heterocyclic rings containing an oxygen atom and 1 to 2 oxygen atoms such as benzoxathiinyl. Heterocyclyl group also include those described above in which one or more S atoms in the ring is double bonded to one or two oxygen atoms (sulfoxides and sulfones). For example, heterocyclyl groups include tetrahydrothiophene, tetrahydrothiophene oxide, and tetrahydrothiophene 1,1-dioxide. Preferred heterocyclyl groups contain 5 or 6 ring members. More preferred heterocyclyl groups include morpholine, piperazine, piperidine, pyrrolidine, pyridine, 2,5-diazabicyclo[2.2.1]heptane, 1-4-diazacycloheptane, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, thiomorpholine, pyrrole, homopiperazine, oxazolidin-2-one, pyrrolidin-2-one, oxazole, thiazole, isoxazole, furan, and tetrahydrofuran.

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The phrase "substituted heterocyclyl" refers to an unsubstituted heterocyclyl group as defined above in which one of the ring members is bonded to a non-hydrogen atom such as described above with respect to substituted alkyl groups and substituted aryl groups. Examples, include, but are not limited to, 2-methylbenzimidazolyl, 5-methylbenzimidazolyl, 5-chlorobenzthiazolyl, 1-methyl piperazinyl, 1-ethylpiperazinyl, 1-isopropylpiperazinyl, 4-(piperidinyl)piperidinyl, 2,6-dimethylpiperazinyl, 3,5-dimethylpiperazinyl, 2,6-dimethylmorpholinyl, dimethyl[(5-methylmorpholin-2-yl)methyl]amine, dimethyl(morpholin-2-ylmethyl)amine, 5-methyl-2-(dimethylaminomethyl)-1-oxa-4-azacycloheptyl, 1-methyl-1,4-diazabicycloheptane, hydroxyalkylpiperazinyl, dialkylaminopyrrolidinyl, alkylpyrrolidinyl, and 2-chloropyridyl among others.

The phrase "unsubstituted heteroaryl" refers to an unsubstituted heterocyclyl group as defined above which is aromatic. Pyridine is just one example of such a group.

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The phrase "substituted heteroaryl" refers to an unsubstituted heteroaryl group as defined above in which a ring member of the heteroaryl group is bonded to a non-hydrogen atom.

The phrase "unsubstituted arylheterocyclyl" refers to heterocyclyl

5 groups as defined above in which a ring member of a heterocyclyl group is bonded
to an otherwise unsubstituted aryl group as defined above. For example, piperazine
is a heterocyclyl group. If a nitrogen or carbon atom of the piperazinyl group is
bonded to an unsubstituted aryl group, then the compound is an unsubstituted
arylheterocyclyl group if the heterocyclyl group is also unsubstituted save for its

10 point of attachment to the parent compound.

The phrase "substituted arylheterocyclyl" refers to heterocyclyl groups as defined above in which a ring member of a heterocyclyl group is bonded to an aryl group as defined above. For example, piperazine is a heterocyclyl group. If a nitrogen or carbon atom of the piperazinyl group is bonded to an aryl group, then the compound is a substituted arylheterocyclyl group if the aryl group is otherwise substituted and/or the heterocyclyl group is also substituted in addition to its point of attachment to the parent compound.

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The phrase "unsubstituted cycloalkylheterocyclyl" refers to heterocyclyl groups as defined above in which a ring member of a heterocyclyl group is bonded to an otherwise unsubstituted cycloalkyl group. For example, piperazine is a heterocyclyl group. If a nitrogen or carbon atom of the piperazinyl group is bonded to an unsubstituted cycloalkyl group, then the compound is an unsubstituted cycloalkylheterocyclyl group if the heterocyclyl group is also unsubstituted save for its point of attachment to the parent compound. Unsubstituted cycloalkylheterocyclyl groups include, but are not limited to N-cyclohexylpiperazinyl groups, 4-(cyclohexyl)piperidinyl groups, 4-cyclopentylpiperidinyl groups, and the like.

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The phrase "substituted cycloalkylheterocyclyl" refers to heterocyclyl groups as defined above in which a ring member of a heterocyclyl group is bonded to a cycloalkyl group as defined above. For example, piperazine is a heterocyclyl group. If a nitrogen or carbon atom of the piperazinyl group is bonded to a cycloalkyl group, then the compound is a substituted cycloalkylheterocyclyl group if the cycloalkyl group is otherwise substituted and/or the heterocyclyl group is also substituted in addition to its point of attachment to the parent compound.

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The phrase "unsubstituted heterocyclylheterocyclyl" refers to heterocyclyl groups as defined above in which a ring member of a first heterocyclyl group is bonded to a second otherwise unsubstituted heterocyclyl group as defined above. For example, piperazine is a heterocyclyl group. If a nitrogen or carbon atom of the piperazinyl group is bonded to a second unsubstituted heterocyclyl group, then the compound is an unsubstituted heterocyclylheterocyclyl group if the first heterocyclyl group is otherwise unsubstituted save for its point of attachment to the parent compound. Unsubstituted heterocyclylheterocyclyl groups include, among others piperidinylpiperidinyl groups and the like such as, but not limited to, 4-(piperidinyl)piperidinyl.

The phrase "substituted heterocyclylheterocyclyl" refers to heterocyclyl groups as defined above in which a ring member of a first heterocyclyl group is bonded to a second heterocyclyl group as defined above. For example, piperazine is a heterocyclyl group. If a nitrogen or carbon atom of the piperazinyl group is bonded to a second heterocyclyl group, then the compound is a substituted heterocyclylheterocyclyl group if the second heterocyclyl group is otherwise substituted and/or the first heterocyclyl group is also substituted in addition to its point of attachment to the parent compound.

The phrase "unsubstituted heterocyclylalkyl" refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to a an otherwise unsubstituted heterocyclyl group as defined above. For example, methyl

(-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to an unsubstituted heterocyclyl group, such as if the carbon of the methyl were bonded to carbon 2 of pyridine (one of the carbons bonded to the N of the pyridine) or carbons 3 or 4 of the pyridine, then the compound is an unsubstituted heterocyclylalkyl group.

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The phrase "substituted heterocyclylalkyl" has the same meaning with respect to unsubstituted heterocyclylalkyl groups that substituted arylalkyl groups had with respect to unsubstituted arylalkyl groups. However, a substituted heterocyclylalkyl group also includes groups in which a non-hydrogen atom is bonded to a heteroatom in the heterocyclyl group of the heterocyclylalkyl group such as, but not limited to, a nitrogen atom in the piperidine ring of a piperidinylalkyl group.

The phrase "unsubstituted alkoxy" refers to an -O-alkyl group where the alkyl group is otherwise unsubstituted. Examples of unsubstituted alkoxy groups include, but are not limited to methoxy, ethoxy, n-propoxy, i-propoxy, and n-butoxy groups.

The phrase "substituted alkoxy" refers to an -O-alkyl group where the alkyl group is otherwise substituted.

The phrase "unsubstituted aryloxy" refers to an -O-aryl group where
the aryl group is otherwise unsubstituted. Examples of unsubstituted aryloxy groups include, but are not limited to, phenyloxy, and naphthyloxy groups.

The phrase "substituted aryloxy" refers to an -O-aryl group where the aryl group is otherwise substituted. Examples of such groups include 4-chlorophenyloxy and 2-methylphenyloxy groups.

The phrase "unsubstituted heterocyclyloxy" refers to an -O-heterocyclyl group where the heterocyclyl group is otherwise unsubstituted.

The phrase "substituted heterocyclyloxy" refers to an -O-heterocyclyl group where the heterocyclyl group is otherwise substituted.

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The phrase "unsubstituted arylalkoxy" refers to an arylalkyl-O- group where the alkyl group of the arylalkyl group is bonded to the O atom and the arylalkyl group is otherwise unsubstituted.

The phrase "substituted arylalkoxy" refers to an arylalkyl-O- group where the alkyl group of the arylalkyl group is bonded to the O atom and the arylalkyl group is otherwise substituted.

The phrase "unsubstituted heterocyclylalkoxy" refers to a

10 heterocyclylalkyl-O- group where the alkyl group of the heterocycylalkyl group is
bonded to the O atom and the heterocyclylalkyl group is otherwise unsubstituted.

The phrase "substituted heterocyclylalkoxy" refers to an heterocyclylalkyl-O- group where the alkyl group of the heterocyclylalkyl group is bonded to the O atom and the heterocyclylalkyl group is otherwise substituted.

The phrase "unsubstituted alkoxyalkoxy" refers to an -O-alkyl-O-alkyl group where both of the alkyl groups are otherwise unsubstituted.

The phrase "substituted alkoxyalkoxy" refers to an -O-alkyl-O-alkyl group where one or both of the alkyl groups are otherwise substituted.

The phrase "unsubstituted amino" refers to -NH2.

The phrase "substituted amino" refers to an amino group in which one or more bonds to the hydrogen atoms of the amino group are replaced by bonds to non-hydrogen atom. Examples of substituted amino groups include, but are not limited to, substituted and unsubstituted alkylamino groups, heterocyclylamino groups, arylamino groups, dialkylamino groups, diheterocyclylamino groups, diarylamino groups, (alkyl)(heterocycyl)amino groups, (alkyl)(aryl)amino groups, and (heterocyclyl)(aryl) groups.

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The phrase "unsubstituted alkylamino" refers to an amino group in which one of the bonds to one of the hydrogen atoms in the amino group is replaced with a bond to an otherwise unsubstituted alkyl group as defined above. Examples of unsubstituted alkylamino groups include, but are not limited to, methylamino, ethylamino, i-propylamino, n-propylamino, butylamino, and cyclohexylamino groups.

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The phrase "substituted alkylamino" refers to an amino group in which one of the bonds to one of the hydrogen atoms in the amino group is replaced with a bond to an otherwise substituted alkyl group as defined above.

The phrase "unsubstituted heterocyclylamino" refers to an amino group in which one of the bonds to one of the hydrogen atoms in the amino group is replaced with a bond to an otherwise unsubstituted heterocyclyl group as defined above.

The phrase "substituted heterocyclylamino" refers to an amino group in which one of the bonds to one of the hydrogen atoms in the amino group is replaced with a bond to an otherwise substituted heterocyclyl group as defined above.

The phrase "unsubstituted dialkylamino" refers to an amino group in which the bonds to the two hydrogen atoms in the amino group are replaced with bonds to two alkyl groups which may be the same or different and which are otherwise unsubstituted alkyl groups as defined above. Examples of unsubstituted dialkylamino groups include, but are not limited to, dimethylamino groups, (methyl)(ethyl)amino groups, and (methyl)(cyclohexyl)amino groups where the parentheses in groups such as (methyl)(cyclohexyl)amino group indicate that the methyl group is bonded to the nitrogen atom of the amino group and the cyclohexyl group is bonded to the nitrogen atom of the amino group.

The phrase "substituted dialkylamino" refers to an amino group in which the bonds to the two hydrogen atoms in the amino group are replaced with

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bonds to two alkyl groups which may be the same or different. Furthermore, in substituted dialkylamino groups, at least one of two alkyl groups is an otherwise substituted alkyl group as defined above.

The phrase "unsubstituted (alkyl)(heterocyclyl)amino" refers to an

amino group in which one of the bonds to one of the hydrogen atoms of the amino
group is replaced by a bond to an otherwise unsubstituted alkyl group as defined
above and the bond to the other hydrogen atom of the amino group is replaced by a
bond to an otherwise unsubstituted heterocyclyl group. Examples of unsubstituted
(alkyl)(heterocyclyl)amino groups include, but are not limited to,
(methyl)(pyridyl)amino groups, (methyl)(morpholinyl)amino groups, and
(methyl)(piperidinyl)amino groups.

The phrase "substituted (alkyl)(heterocyclyl)amino" refers to an amino group in which one of the bonds to one of the hydrogen atoms of the amino group is replaced by a bond to an otherwise substituted or unsubstituted alkyl group as defined above and the bond to the other hydrogen atom of the amino group is replaced by a bond to an otherwise substituted or unsubstituted heterocyclyl group. However, if the bond to one of the hydrogen atoms in the amino group is replaced by a bond to an otherwise unsubstituted alkyl group, then the bond to the other hydrogen atom of the amino group is replaced by a bond to an otherwise substituted heterocyclyl group. The reverse is also true so that the alkyl group and/or the heterocyclyl group is substituted in a substituted (alkyl)(heterocyclyl)amino group.

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The phrase "unsubstituted heterocyclylalkylamino" refers to an amino group in which a bond to one of the hydrogen atoms in the amino group is replaced with a bond to the alkyl group of an otherwise unsubstituted heterocyclylalkyl group. Examples of unsubstituted heterocyclylalkylamino groups include, but are not limited to, 3-pyridylmethylamino, 1-piperidinylmethylamino, and 4-morpholinylmethylamino groups.

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The phrase "substituted heterocyclylalkylamino" refers to an amino group in which a bond to one of the hydrogen atoms in the amino group is replaced with a bond to the alkyl group of an otherwise substituted heterocyclylalkyl group.

The phrase "unsubstituted arylalkylamino" refers to an amino group in which a bond to one of the hydrogen atoms in the amino group is replaced with a bond to the alkyl group of an otherwise unsubstituted arylalkyl group. Examples of unsubstituted arylalkylamino groups include, but are not limited to, phenylmethylamino, and naphthylethylamino groups.

The phrase "substituted arylalkylamino" refers to an amino group in which a bond to one of the hydrogen atoms in the amino group is replaced with a bond to the alkyl group of an otherwise substituted arylalkyl group.

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The term "protected" with respect to hydroxyl groups, amine groups, and sulfhydryl groups refers to forms of these functionalities which are protected from undesirable reaction with a protecting group known to those skilled in the art such as those set forth in Protective Groups in Organic Synthesis, Greene, T.W., John Wiley & Sons, New York, NY, (1st Edition, 1981) which can be added or removed using the procedures set forth therein. Examples of protected hydroxyl groups include, but are not limited to, silyl ethers such as those obtained by reaction of a hydroxyl group with a reagent such as, but not limited to, t-butyldimethylchlorosilane, trimethylchlorosilane, triisopropylchlorosilane, triethylchlorosilane; substituted methyl and ethyl ethers such as, but not limited to methoxymethyl ether, methythiomethyl ether, benzyloxymethyl ether, t-butoxymethyl ether, 2methoxyethoxymethyl ether, tetrahydropyranyl ethers, 1-ethoxyethyl ether, allyl ether, benzyl ether; esters such as, but not limited to, benzoylformate, formate, acetate, trichloroacetate, and trifluoracetate. Examples of protected amine groups include, but are not limited to, amides such as, formamide, acetamide, trifluoroacetamide, and benzamide; imides, such as phthalimide, and dithiosuccinimide; and others. Examples of protected sulfhydryl groups include, but are not limited to, thioethers such as S-benzyl thioether, and S-4-picolyl thioether;

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substituted S-methyl derivatives such as hemithio, dithio and aminothio acetals; and others.

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A "pharmaceutically acceptable salt" includes a salt with an inorganic base, organic base, inorganic acid, organic acid, or basic or acidic amino acid. As salts of inorganic bases, the invention includes, for example, alkali metals such as sodium or potassium; alkaline earth metals such as calcium and magnesium or aluminum; and ammonia. As salts of organic bases, the invention includes, for example, trimethylamine, triethylamine, pyridine, picoline, ethanolamine, diethanolamine, and triethanolamine. As salts of inorganic acids, the instant invention includes, for example, hydrochloric acid, hydroboric acid, nitric acid, sulfuric acid, and phosphoric acid. As salts of organic acids, the instant invention includes, for example, formic acid, acetic acid, trifluoroacetic acid, fumaric acid, oxalic acid, tartaric acid, maleic acid, citric acid, succinic acid, malic acid, methanesulfonic acid, benzenesulfonic acid, and p-toluenesulfonic acid. As salts of basic amino acids, the instant invention includes, for example, arginine, lysine and ornithine. Acidic amino acids include, for example, aspartic acid and glutamic acid.

The present invention provides compounds, pharmaceutical formulations including the compounds, methods of preparing the pharmaceutical formulations, and methods of treating patients with the pharmaceutical formulations and compounds.

The present invention provides compounds having the structure I. The invention also provides tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure I has the following formula:

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$$R^{5}$$
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{10}
 Z^{10}

where, in the first group of compounds:

 Z^1 , Z^2 , Z^3 , and Z^4 are selected independently from C or N;

R¹-R⁸ are selected independently from the group consisting of -H, -F, -Cl, -Br, -C=N, -NO₂, -CF₃, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups. substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted 10 heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted alkylheterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heteroaryl groups, substituted and unsubstituted -C(=0)-N(H)-heterocyclyl groups, substituted and unsubstituted -15 C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and

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unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heteroaryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted heterocyclyl groups;

$$R^9$$
 is -H, -C(=O)-alkyl, or -C(=O)-aryl; and R^{10} is -H, -C(=O)-alkyl, or -C(=O)-aryl.

More particular embodiments of the compounds of the invention having the general structure shown in I above are provided. The second group of compounds are those for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

R¹ is selected from -H, -F, -Cl, and -Br;

R² is selected from -H, -F, -Cl, -Br, -C≡N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and

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unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted heterocyclylalkoxy groups;

R³ is selected from -H, -F, -Cl, -Br, and substituted and unsubstituted alkoxy groups;

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 R^5 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^5 is absent if Z^1 is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, and substituted and unsubstituted -C(=O)N(H)heterocyclyl groups; or R⁶ is absent if Z² is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including

substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl 5 groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted 10 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, and substituted and unsubstituted -C(=O)N(H)heterocyclyl groups; or R⁷ is absent if Z³ is N;

R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

 R^9 is -H; and

 R^{10} is -H. In some embodiments of the second group of compounds, at least one of R^1 , R^2 , R^3 , R^5 , R^6 , R^7 or R^8 is not -H. In other such embodiments, at least two of R^1 , R^2 , R^3 , R^5 , R^6 , R^7 or R^8 are not -H.

In one embodiment of the second group of compounds, each of Z^1 , Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the second group of compounds, Z^1 is N and each of Z^2 , Z^3 , and Z^4 are C.

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In another embodiment of the second group of compounds, Z^1 and Z^3 are both N and Z^2 and Z^4 are both C.

In another embodiment of the second group of compounds, Z^3 is N and each of Z^1 , Z^2 , and Z^4 are C.

In another embodiment of the second group of compounds, Z¹-Z⁴ have any of the values in previous embodiments, and R¹ is selected from -H, -F, -Cl, and -Br.

In another embodiment of the second group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is selected from -H, -F, -Cl, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted and

In another embodiment of the second group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is -H.

In another embodiment of the second group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is an unsubstituted alkoxy group having from 1 to 4 carbon atoms.

In another embodiment of the second group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is -OMe.

In another embodiment of the second group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is -O-i-Pr.

In another embodiment of the second group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted arylalkoxy group.

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In another embodiment of the second group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a benzyloxy group.

In another embodiment of the second group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is an unsubstituted alkyl group having from 1 to 4 carbon atoms.

In another embodiment of the second group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a methyl group.

In another embodiment of the second group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from -H, -F, -Cl, and -OMe.

In another embodiment of the second group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from -F, -Cl, -Br, and substituted and unsubstituted alkoxy groups.

In another embodiment of the second group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -H.

In another embodiment of the second group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -F.

In another embodiment of the second group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -C1.

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In another embodiment of the second group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -OMe.

In another embodiment of the second group of compounds, Z^2-Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is H.

In another embodiment of the second group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is -CH₃.

In another embodiment of the second group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is morpholine.

In another embodiment of the second group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is H.

In another embodiment of the second group of compounds, Z^1-Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is -CH₃.

In another embodiment of the second group of compounds, Z¹-Z³, R¹, R², and R³ have any of the values in previous embodiments, Z⁴ is C, and R⁸ is morpholine.

In another embodiment of the second group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from -Br, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted

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and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted

heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other such embodiments, R⁶ has the values described in the preceding sentence and R⁷ is -H.

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In another embodiment of the second group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R^6 is a methoxy group. In still other such embodiments where R^6 is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R^7 is -H.

In another embodiment of the second group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R⁶ is a methyl group. In still other such embodiments where R⁶ is an alkyl group having from 1-6 carbon atoms such as a methyl group, R⁷ is -H.

In another embodiment of the second group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted alkoxy group having the formula -OCH₂(CH₂)_mR¹¹ where m is an integer selected from 0, 1, or 2 and R¹¹ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In still other such embodiments, R¹¹ is selected from substituted alkoxy groups. In still other such embodiments, R¹¹ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other such embodiments where R⁶ is a substituted alkoxy group having the formula -OCH₂(CH₂)_mR¹¹, R⁷ is -H.

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In another embodiment of the second group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted amino group having the formula -N(R¹²)CH₂(CH₂)_mR¹³ where m is an integer selected from 0, 1, or 2, R¹³ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is -H or a substituted or unsubstituted alkyl group. In some such embodiments R¹² is H. In other embodiments R¹² is a -CH₃ group. In still other such embodiments, R¹³ is selected from substituted alkoxy groups. In still other such embodiments, R¹³ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups.

In still other embodiments of the second group of compounds where R^6 is a substituted amino group having the formula $-N(R^{12})CH_2(CH_2)_mR^{13}$, R^7 is -H.

15 In another embodiment of the second group of compounds, Z^1 , Z^3 , Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values defined in the previous embodiments, Z² is C, and R⁶ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the second group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted 20 pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted 2.5diazabicyclo[2.2.1]heptane groups, and substituted and unsubstituted 1,4diazabicyclo[2.2.2]octane groups. In other embodiments of the second group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is an 25 unsubstituted morpholine group, a dialkyl substituted morpholinyl group, an unsubstituted piperazine group, a dialkyl substituted piperazinyl group, a monoalkyl substituted piperazinyl group, an aryl substituted piperazinyl group, a -CH₂C(=O)O-alkyl substituted piperazinyl group, a -C(=O)-alkyl substituted

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piperazinyl group, a -C(=O)O-alkyl substituted piperazinyl group, a cycloalkyl substituted piperazinyl group, an unsubstituted piperidine group, an aryl substituted piperidinyl group, a cycloalkyl substituted piperidinyl group, a piperidinyl substituted piperidinyl group, a dialkylamino substituted pyrrolidinyl group, an unsubstituted 2,5-diazabicyclo[2.2.1]heptane group, and an alkyl substituted 2,5-diazabicyclo[2.2.1]heptane group. In still other embodiments of the second group of compounds where R^6 is a substituted or unsubstituted heterocyclyl group, R^7 is -H.

In another embodiment of the second group of compounds, Z^1 , Z^2 , Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, 10 and R⁷ is selected from substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted 15 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted 20 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, 25 and substituted and unsubstituted heterocyclylamino groups. In still other such embodiments, R⁷ has the values described in the preceding sentence and R⁶ is -H.

In another embodiment of the second group of compounds, Z^1 , Z^2 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^3 is C, and R^7 is an alkoxy group having from 1-6 carbon atoms. In still other such

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embodiments, R^7 is a methoxy group. In still other embodiments of the second group of compounds where R^7 is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R^6 is -H.

In another embodiment of the second group of compounds, Z^1 , Z^2 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^3 is C, and R^7 is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R^7 is a methyl group. In still other embodiments of the second group of compounds where R^7 is an alkyl group having from 1-6 carbon atoms such as a methyl group, R^6 is -H.

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In another embodiment of the second group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴ where n is an integer selected from 0, 1, or 2 and R¹⁴ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In still other such embodiments, R¹⁴ is selected from substituted alkoxy groups. In still other such embodiments, R¹⁴ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments of the second group of compounds where R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴, R⁶ is -H.

In another embodiment of the second group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)CH₂(CH₂)_nR¹⁶ where n is an integer selected from 0, 1, or 2, R¹⁶ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹⁵ is selected from -H and alkyl groups. In some such embodiments, R¹⁵ is a -H group. In other such embodiments, R¹⁵ is a -CH₃ group. In still other such embodiments, R¹⁶ is selected

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from substituted alkoxy groups. In still other such embodiments, R¹⁶ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups.

In still other embodiments of the second group of compounds where R^7 is a substituted amino group having the formula $-N(R^{15})CH_2(CH_2)_nR^{16}$, R^6 is -H.

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In another embodiment of the second group of compounds, Z^1 , Z^2 . Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted or unsubstituted heterocyclyl group. In some such embodiments where R⁷ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted 2,5-diazabicyclo[2,2,1]heptane groups, and substituted and unsubstituted 1,4-diazabicyclo[2.2.2]octane groups. In still other embodiments of the second group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group, a dialkyl substituted morpholinyl group, an unsubstituted piperazine group, a dialkyl substituted piperazinyl group, a monoalkyl substituted piperazinyl group, an aryl substituted piperazinyl group, a -CH₂C(=O)O-alkyl substituted piperazinyl group, a -C(=O)alkyl substituted piperazinyl group, a -C(=0)O-alkyl substituted piperazinyl group, a cycloalkyl substituted piperazinyl group, an unsubstituted piperidine group, an aryl substituted piperidinyl group, a cycloalkyl substituted piperidinyl group, a piperidinyl substituted piperidinyl group, a dialkylamino substituted pyrrolidinyl group, an unsubstituted 2,5-diazabicyclo[2.2.1]heptane group, and an alkyl substituted 2,5-diazabicyclo[2.2.1]heptane group. In still other embodiments of the second group of compounds where R⁷ is a substituted or unsubstituted heterocyclyl group, R⁶ is -H.

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Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a third group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

5 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C \equiv N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=0)-arvl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 10 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 15 groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 20 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl 25 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups,

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substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^2 is selected from -H, -F, -Cl, -Br, -C=N, -NO₂, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, 10 substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups substituted and unsubstituted -C(=O)N(H)aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=0)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-15 heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=0)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, 20 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and 25 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 30

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(alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH2O-such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms:

R³ is selected from -H, -F, -Cl, -Br, -CF3, -C=N, substituted and unsubstituted alkyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO2)-aryl groups, -N(H)-(SO2)-CF3 groups, substituted and unsubstituted -N(H)-(SO2)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-C(=O)N(H)-aryl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups, substituted and unsubstituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted

(alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl

heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups;

 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted 10 heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=0)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, 15 -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups. 20 substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 25 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 30 unsubstituted arylaminoalkyl groups, substituted and unsubstituted

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heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

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R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

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-C(=0)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl) (heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁷ is absent if Z³ is N;

 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R9 is -H; and

R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups. In some such embodiments of the third group of

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compounds, at least one of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 or R^8 is not –H. In other such embodiments, at least two of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 or R^8 are not –H. In some embodiments, R^{10} is –H. In other embodiments, R^{10} is an unsubstituted alkyl group having from 1 to 6 carbon atoms such as a methyl, ethyl, propyl, i-propyl group, or the like. In some such embodiments, R^{10} is a –CH₃ group.

In one embodiment of the third group of compounds, each of Z^1 , Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the third group of compounds, Z^1 is N and each of Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the third group of compounds, Z^1 and Z^3 are both N and Z^2 and Z^4 are both C.

In another embodiment of the third group of compounds, Z^3 is N and each of Z^1 , Z^2 , and Z^4 are C.

In another embodiment of the third group of compounds, Z¹-Z⁴ have
any of the values in previous embodiments, and R¹ is selected from -H, -F, -C1, and
-Br.

In another embodiment of the third group of compounds, Z¹-Z⁴ have any of the values in previous embodiments, and R¹ is a substituted and unsubstituted heterocyclylamino group. In some such embodiments, R¹ is a substituted and unsubstituted heteroarylamino groups. In some embodiments, R¹ is a substituted and unsubstituted heterocyclylamino group such as, but not limited to, substituted and unsubstituted pyrroldinylalkylamino groups and the like, such as, but not limited to, substituted and unsubstituted pyrroldinylamino groups and the like.

In another embodiment of the third group of compounds, Z¹-Z⁴ and
R¹ have any of the values in previous embodiments, and R² is selected from -H, -F,
-Cl, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted
-C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups,

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substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted heterocyclylalkoxy groups; or R^2 and R^3 are a group of formula - OCH_2O - such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the third group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is -H.

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In another embodiment of the third group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is an unsubstituted alkoxy group having from 1 to 4 carbon atoms.

In another embodiment of the third group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a -OMe, -OEt, -O-i-Pr, or -OCH₂CH(CH₃)₂ group.

In another embodiment of the third group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted arylalkoxy, a substituted or unsubstituted aryloxy group, or a substituted or unsubstituted heterocyclyoxy group.

In another embodiment of the third group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted benzyloxy group, a substituted or unsubstituted phenoxy group, or a substituted or unsubstituted pyridyloxy group.

In another embodiment of the third group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is an unsubstituted alkyl group having from 1 to 4 carbon atoms.

In another embodiment of the third group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a methyl group.

In another embodiment of the third group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted -N(H)C(=O)-N(H)-alkyl-aryl group.

In another embodiment of the third group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or 10 unsubstituted amino group selected from the group consisting of substituted and unsubstituted alkylamino groups, dialkylamino groups, cycloalkylamino groups, heterocyclylamino groups, heterocyclylalkylamino groups, arylalkylamino groups, arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups. In some 15 embodiments, the substituted and unsubstituted alkylamino groups are substituted and unsubstituted aminoalkylamino groups such as, but not limited to, dialkylaminoalkylamino and the like. In some such embodiments the substituted and unsubstituted heterocyclylalkylamino groups are substituted and unsubstituted heteroarylalkylamino groups. In some embodiments, the heterocyclylalkylamino 20 groups include, but are not limited to, substituted and unsubstituted pyrrolidinylalkylamino groups such as, but not limited to, substituted and unsubstituted pyrrolidinylmethylalkylamino groups and the like; substituted and unsubstituted thiazolylalkylamino groups such as, but not limited to substituted and unsubstituted thiazolylmethylamino groups and the like; substituted and 25 unsubstituted imidazolylalkylamino groups such as, but not limited to, imidazolylmethylamino groups and the like; substituted and unsubstituted furanylalkylamino groups such as, but not limited to, substituted and unsubstituted furanylmethylamino groups, and the like; and the like. In other such embodiments, the heterocyclylamino groups are substituted and unsubstituted heteroarylamino

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groups. In other such embodiments, the substituted and unsubstituted heterocyclylamino groups are substituted and unsubstituted arylalkylheterocyclylamino groups.

In another embodiment of the third group of compounds, Z¹-Z⁴ and

R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of isopropylamino groups, 3-(N,N-dimethylamino)propylamino groups, pyrrolidinylmethylamino groups, arylmethylamino groups, arylalkoxyarylmethylamino groups, aryloxyarylmethylamino groups, and pyridylmethylamino groups, and pyridylamino groups.

groups.

In another embodiment of the third group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted heterocyclyl groups. In some such embodiments R^2 is a substituted or unsubstituted benzimidazolyl group or is a substituted or unsubstituted pyrazolyl group.

In another embodiment of the third group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the third group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is selected from -H, -F, -Cl, and -OMe.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -H.

In another embodiment of the third group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is selected from the group consisting of -F, -Cl, -Br, -C≡N, substituted and unsubstituted alkyl

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groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted – N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups; or R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)CH₂CH₃ group, a substituted or unsubstituted -N(H)C(=O)N(H)CH(CH₃)₂ group, a substituted or unsubstituted -N(H)C(=O)N(H)C(CH₃)₃ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group, a-N(H)C(=O)N(H)-(trifluoromethylphenyl) group, or the like.

In another embodiment of the third group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -F.

In another embodiment of the third group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -C1.

In another embodiment of the third group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -OMe.

In some embodiments of the third group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and if R³ is H, at least one of R⁶ or R⁷ is selected from the group consisting of -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted cycloalkylheterocyclyl

groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted -N(H)-alkyl groups, substituted and unsubstituted -N(H)-alkylheterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups. In some such embodiments, if R^3 is H, at least one of R^6 or R^7 is selected from the group consisting of $-CO_2H$, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups.

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In another embodiment of the third group of compounds, Z²-Z⁴, R¹, R², and R³ have any of the values in previous embodiments, Z¹ is C, and R⁵ is H.

In some such embodiments, R⁸ is also H.

In another embodiment of the third group of compounds, Z^2-Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is -CH₃.

In another embodiment of the third group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is morpholine.

In another embodiment of the third group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is H.

In another embodiment of the third group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is -CH₃.

In another embodiment of the third group of compounds, Z¹-Z³, R¹, R², and R³ have any of the values in previous embodiments, Z⁴ is C, and R⁸ is morpholine.

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In another embodiment of the third group of compounds, Z¹, Z³, Z⁴. R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from a first group of compounds; or Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from 5 the first group of compounds, the first group of compounds comprising members selected from the group consisting of -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups. substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl 10 groups, substituted and unsubstituted cycloalkylheterocyclyl groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, -C(=O)N(H)-heteroaryl groups, substituted 15 and unsubstituted -C(=O)N(alkyl) (heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups.

In another embodiment of the third group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from -Br, substituted and unsubstituted alkyl groups, substituted and 20 unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups. 25 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=0)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl 30

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groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other embodiments, R⁶ has the values described in the preceding sentence and R⁷ is -H.

In another embodiment of the third group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R^6 is a methoxy group. In still other embodiments of the third group of compounds where R^6 is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R^7 is -H.

In another embodiment of the third group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R⁶ is a methyl group. In still other embodiments of the third group of compounds where R⁶ is an alkyl group having from 1-6 carbon atoms such as a methyl group, R⁷ is -H.

In another embodiment of the third group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted alkoxy group having the formula -OCH₂(CH₂)_mR¹¹ where m is an integer selected from 0, 1, or 2 and R¹¹ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In still other such embodiments, R¹¹ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹¹ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl

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groups, and piperidinyl groups. In still other embodiments where R⁶ is a substituted alkoxy group having the formula $-OCH_2(CH_2)_mR^{11}$, R⁷ is -H. In still other embodiments, R⁶ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3-pyridinyl)methoxy groups, or the like.

In another embodiment of the third group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted amino group having the formula -N(R¹²)(CH₂)₀R¹³ where p is an 10 integer selected from 0, 1, 2, or 3, R¹³ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H or substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl. In some such embodiments, R¹³ is 15 selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R12 is a CH3 group. In still other such embodiments, R¹³ is selected from substituted alkoxy groups. In still other such 20 embodiments, R¹³ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some embodiments, R⁶ is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1-25 methylpiperidinyl)) groups, -N(H)CH2(2-pyridyl) groups, -N(H)CH2(3-pyridyl) groups, -N(H)CH2(4-pyridyl) groups, -N(H)CH2CH2(2-pyridyl) groups, -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups. -N(CH₃)CH₂CH₂(2-pyridyl) groups -N(H)CH₂CH₂(4-piperidinyl) groups, -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, 30

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-N(H)CH₂CH₂(1-(4-methylpiperazinyl)) groups, -N(H)CH₂CH₂(4-morpholinyl) groups, -N(H)CH₂CH₂CH₂(1-imidazolyl) groups, -N(H)CH₂CH₂(1-pyrrolidinyl) groups, -N(CH₃)CH₂CH₂CH₂(diethylamino) groups, and the like.

In still other embodiments of the third group of compounds where R^6 is a substituted amino group having the formula $-N(R^{12})(CH_2)_pR^{13}$, R^7 is -H.

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In another embodiment of the third group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted amino group having the formula -N(R¹²)(CH₂)₀R¹³ or the formula $-N(R^{12})C(H)(alkyl)((CH_2)_pR^{13})$ where p is an integer selected from 0, 1, 2, or 3, R^{13} 10 is selected from a methyl group, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)₂ groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and 15 isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₃ groups and the like; -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(alkyl)2 groups such as -C(=O)-CH2-N(alkyl)2 groups and the like; -C(=O)-alkyl- $N(R^{12a'})(R^{12b'})$ groups such as -C(=O)-CH₂- $N(alkyl)_2$ groups and the like -C(=O)-alkyl-heterocyclyl groups such as -C(=O)-CH₂-heterocyclyl groups 20 and the like such as -C(=O)-CH₂-(1-piperazinyl) groups and the like; -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{12a'} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{12b'} is selected from -H, 25 -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=O)-alkyl-halogen groups.

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In another embodiment of the third group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values defined in the previous embodiments, Z² is C, and R⁶ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the third group of compounds where R⁶ is a heterocyclyl group, the 5 heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups. substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted pyrazolyl groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted 10 imidazolyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2,5-diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4-diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1.4-diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 15 1,4-diazacycloheptane groups. In still other embodiments of the third group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy 20 substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the 25 ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group 30

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and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, 10 and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl substituted piperazinyl group; a -C(=0)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-ethyl or a -C(=0)-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-ethyl or the -15 C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z^2 , and the like; a -C(=O)O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=0)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z², and the like; a cycloalkyl substituted piperazinyl 20 group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4-25 hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to. 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like 30

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such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a 10 heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as, but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such 15 as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a 20 hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2,5diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 25 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0] nonane group; and a substituted or unsubstituted 1,4diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still 30

other embodiments of the third group of compounds where R^6 is a substituted or unsubstituted heterocyclyl group, R^7 is -H.

In another embodiment of the third group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, 10 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=0)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arytheterocyclyl groups, substituted and unsubstituted 15 alkylheterocyclyl groups and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted 20 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other such embodiments, R⁷ has the values described in the preceding sentence and R⁶ is -H.

In another embodiment of the third group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R⁷ is a methoxy group. In still other embodiments of the third group of compounds where R⁷ is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R⁶ is -H.

In another embodiment of the third group of compounds, Z^1 , Z^2 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^3 is C, and R^7 is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R^7 is a methyl group. In still other embodiments of the third group of compounds where R^7 is an alkyl group having from 1-6 carbon atoms such as a methyl group, R^6 is -H.

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In another embodiment of the third group of compounds, Z^1 , Z^2 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴ where n is an integer selected from 0, 1, or 2 and R14 is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In some embodiments, R¹⁴ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹⁴ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments of the third group of compounds where R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴, R⁶ is -H. In still other embodiments, R⁷ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3pyridinyl)methoxy groups, or the like.

In another embodiment of the third group of compounds, Z¹, Z², Z⁴, Z⁵, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)_qR¹⁶ where q is an integer selected from 0, 1, 2, or 3 and R¹⁶ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted heterocyclyl groups,

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and R¹⁵ is -H or a substituted or unsubstituted alkyl groups, such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups. In some such embodiments, R¹⁶ is selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, 5 (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R¹⁵ is a CH₃ group. In still other such embodiments, R¹⁶ is selected from substituted alkoxy groups. In still other such embodiments, R¹⁶ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups. 10 morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some embodiments, R⁷ is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1methylpiperidinyl)) groups, -N(H)CH₂(2-pyridyl) groups, -N(H)CH₂(3-pyridyl) groups, -N(H)CH2(4-pyridyl) groups, -N(H)CH2CH2(2-pyridyl) groups, -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups, 15 -N(CH₃)CH₂CH₂(2-pyridyl) groups -N(H)CH₂CH₂(4-piperidinyl) groups, -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2(1-imidazolyl) groups, -N(H)CH2CH2CH2(1-(4-methylpiperazinyl)) groups, -N(H)CH2CH2CH2(4-

20 -N(H)CH₂CH₂(1-pyrrolidinyl) groups, -N(CH₃)CH₂CH₂CH₂(diethylamino) groups, and the like.

morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups,

In still other embodiments of the third group of compounds where R^7 is a substituted amino group having the formula- $N(R^{15})(CH_2)_qR^{16}$, R^6 is -H.

In another embodiment of the third group of compounds, Z¹, Z³, Z⁴,

R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and

R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)_qR¹⁶ or the formula

-N(R¹⁵)C(H)(alkyl)((CH₂)_qR¹⁶) where q is an integer selected from 0, 1, 2, or 3, R¹⁶ is selected from a methyl group, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)₂

groups, and -C(=O)-alkyl-halogen groups.

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groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹⁵ is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(R^{15a})(R^{15b}) groups such as -C(=O)-CH₂-N(alkyl)₂ groups and the like -C(=O)-alkyl-heterocyclyl groups such as -C(=O)-CH₂-heterocyclyl groups and the like such as -C(=O)-CH₂-(1-piperazinyl) groups and the like; -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{15a} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{15b} is selected from -H, -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups, alkyl

In another embodiment of the third group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the third group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted and unsubstituted indiazolyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 2,5-diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4-diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4-

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diazacycloheptane groups. In still other embodiments of the third group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as. but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl substituted piperazinyl group; a -C(=O)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-ethyl or a -C(=0)-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=0)-ethyl or the -

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C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to \mathbb{Z}^3 , and the like; a $-\mathbb{C}(=0)$ O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=O)-O-ethyl or a -C(=O)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-Oethyl or the -C(=O)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as. but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such

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as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl 5 group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 10 2,5-diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2,2,1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4-diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4-diazacycloheptane group and the like, such as, but not limited to, an 15 N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but

not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the third group of compounds where R^7 is a substituted or

unsubstituted heterocyclyl group, R⁶ is -H.

In another embodiment of the third group of compounds, Z¹-Z⁴, R¹,

R², and R³ have any of the values in previous embodiments, and one of R⁶ or R⁷ is a

substituted or unsubstituted pyridyloxy group. In some such embodiments, one of

R⁶ or R⁷ is substituted or unsubstituted 2-pyridyloxy group, a 3-pyridyloxy group,

or a 4-pyridyloxy group. In other such embodiments, one of R⁶ or R⁷ is a (2-N
alkylamido-4-pyridyl)oxy group such as a (2-N-methylamido-4-pyridyl)oxy group or

the like; or a (5-N-alkylamido-3-pyridyl)oxy group such as a (5-N-methylamido-3
pyridyl)oxy group, or the like.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a fourth group of compounds for which:

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 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

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 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl 5 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted 10 -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, 15 substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-20 C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted 25 heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-

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C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^2 is selected from -H. -F. -Cl. -Br. -C \equiv N. -NO₂, -CO₂H. -OH. substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -5 C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl 10 groups, substituted and unsubstituted -N(H)C(=0)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 15 -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups. substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted 20 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted 25 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-30

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heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl

heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-

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C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂O-such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms;

R³ is selected from -H, -F, -Cl, -Br, -CF₃, -C≡N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 15 -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups, 20 substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted 25 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 30

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(alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups;

 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, 10 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl 15 groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups. substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and 20 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-25 C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl 30

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groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^5 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^5 is absent if Z^1 is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl) (heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁶ is absent if Z² is N;

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R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁷ is absent if Z³ is N;

R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

R⁹ is -H; and

25 R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups. In some such embodiments of the fourth group of compounds, at least one of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ is not -H. In other such embodiments, at least two of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ are not -H. In some embodiments, R¹⁰ is -H. In other embodiments, R¹⁰ is an unsubstituted alkyl group

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having from 1 to 6 carbon atoms such as a methyl, ethyl, propyl, i-propyl group, or the like. In some such embodiments, R^{10} is a -CH₃ group

In one embodiment of the fourth group of compounds, each of Z^1 , Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the fourth group of compounds, Z^1 is N and each of Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the fourth group of compounds, Z^1 and Z^3 are both N and Z^2 and Z^4 are both C.

In another embodiment of the fourth group of compounds, Z^3 is N and each of Z^1 , Z^2 , and Z^4 are C.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 have any of the values in previous embodiments, and R^1 is selected from -H, -F, -Cl, and -Br.

In another embodiment of the fourth group of compounds, Z¹-Z⁴ have
any of the values in previous embodiments, and R¹ is a substituted and unsubstituted heterocyclylamino group. In some such embodiments, R¹ is a substituted and unsubstituted heteroarylamino groups. In some embodiments, R¹ is an unsubstituted -NH₂ group or is a substituted or unsubstituted heterocyclylamino group such as, but not limited to, substituted and unsubstituted pyrroldinylalkylamino groups and
the like, such as, but not limited to, substituted and unsubstituted pyrrolidinylmethylamino groups and the like such as, but not limited to, -N(H)-CH₂-(2-pyrrolidinyl) groups and the like.

In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is selected from -H, -F, -C1, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted

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-C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-5 aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen 10 atoms. In another embodiment of the fourth group of compounds, R² is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and unsubstituted pyrrolidinylalkylamino groups, and substituted and unsubstituted aminoalkylamino groups. In other such embodiments, R² is 15 selected from the group consisting of -N(H)-CH₂-(2-thiazolyl) groups, -N(H)-CH₂-(2-pyrroldinyl groups), -N(H)-CH₂CH₂CH₂-N(H)(alkyl) groups, and -NH-CH₂CH₂CH₂-N(alkyl)₂ groups. In still other such embodiments, R² is selected from the group consisting of -N(H)-CH2-(2-thiazolyl) groups, -N(H)-CH2-(2pyrroldinyl groups), -N(H)-CH2CH2CH2-N(H)(CH3) groups, and -NH-CH2CH2CH2-20 N(CH₃)₂ groups.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is -H.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is an unsubstituted alkoxy group having from 1 to 4 carbon atoms.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a -OMe, -OEt, -O-i-Pr, or -OCH₂CH(CH₃)₂ group.

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In another embodiment of the fourth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted arylalkoxy, a substituted or unsubstituted aryloxy group, or a substituted or unsubstituted heterocyclyoxy group.

In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted benzyloxy group, a substituted or unsubstituted phenoxy group, or a substituted or unsubstituted pyridyloxy group.

In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is an unsubstituted alkyl group having from 1 to 4 carbon atoms.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a methyl group.

In another embodiment of the fourth group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted -N(H)C(=O)-N(H)-alkyl-aryl group.

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In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of substituted and unsubstituted alkylamino groups, dialkylamino groups, cycloalkylamino groups, heterocyclylamino groups, arylalkylamino groups, arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups. In some embodiments, the substituted and unsubstituted alkylamino groups are substituted and unsubstituted aminoalkylamino groups such as, but not limited to, dialkylaminoalkylamino and the like. In some such embodiments the substituted and unsubstituted heterocyclylalkylamino groups are substituted and unsubstituted heterocyclylalkylamino groups. In some embodiments, the heterocyclylalkylamino groups include, but are not limited to, substituted and unsubstituted

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pyrrolidinylalkylamino groups such as, but not limited to, substituted and unsubstituted pyrrolidinylmethylalkylamino groups and the like; substituted and unsubstituted thiazolylalkylamino groups such as, but not limited to substituted and unsubstituted thiazolylamino groups and the like; substituted and unsubstituted imidazolylalkylamino groups such as, but not limited to, imidazolylmethylamino groups and the like; substituted and unsubstituted furanylalkylamino groups such as, but not limited to, substituted and unsubstituted furanylmethylamino groups, and the like; and the like. In other such embodiments, the heterocyclylamino groups are substituted and unsubstituted heteroarylamino groups. In other such embodiments, the substituted and unsubstituted heterocyclylamino groups are substituted and unsubstituted arylalkylheterocyclylamino groups.

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In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of isopropylamino groups, 3-(N,N-dimethylamino)propylamino groups, pyrrolidinylmethylamino groups, arylmethylamino groups, arylakoxyarylmethylamino groups, aryloxyarylmethylamino groups, and pyridylmethylamino groups, and pyridylamino groups.

In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted heterocyclyl groups. In some such embodiments R² is a substituted or unsubstituted benzimidazolyl group or is a substituted or unsubstituted pyrazolyl group.

In another embodiment of the fourth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms.

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In another embodiment of the fourth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from -H, -F, -Cl, and -OMe.

In another embodiment of the fourth group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -H.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-aryl groups and substituted and unsubstituted -C(\equiv O)N(H)-alkyl-heterocyclyl groups; or R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)CH₂CH₃ group, a substituted or unsubstituted -N(H)C(=O)N(H)CH(CH₃)₂ group, a substituted or unsubstituted -N(H)C(=O)N(H)C(CH₃)₃ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group,

25 a-N(H)C(=O)N(H)-(trifluoromethylphenyl) group, or the like.

In another embodiment of the fourth group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is a substituted amino group selected from substituted or unsubstituted arylalkylamino groups such

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as, but not limited to, phenylalkylamino groups, (halo)(alkoxy)arylalkylamino groups, such as, but not limited to 2-fluoro-5-methoxyphenylmethylamino groups, monoalkoxyarylalkylamino groups, dialkoxyarylalkylamino groups, and the like, such as, but not limited to, 2,5-dialkoxyarylalkylamino groups and the like such as, but not limited to 2,5-dialkoxyarylmethylamino groups, substituted and

- but not limited to 2,5-dialkoxyarylmethylamino groups, substituted and unsubstituted arylalkoxyarylalkylamino groups such as, but not limited to substituted and unsubstituted arylalkoxyarylmethylamino groups and the like, such as, but not limited to, substituted and unsubstituted arylmethoxyarylmethylamino groups and the like, such as, but not limited to substituted and unsubstituted
- fluoroarylmethoxyarylmethylamino groups and the like, such as, but not limited to, substituted and unsubstituted 4-fluorophenylmethoxyphenyl-methylamino groups and the like; substituted and unsubstituted heterocyclylalkylamino groups including heteroarylalkylamino groups such as, but not limited to substituted and unsubstituted thiazolylalkylamino groups, benzimidazolylalkylamino groups such as, but not
- limited to N-methylbenzimidazolylalkylamino groups and the like, imidazolylalkylamino groups such as, but not limited to phenylimidazolylalkylamino groups, ethylmethylimidazolylalkylamino groups, and the like, substituted and unsubstituted quinolinylalkylamino groups, such as, but not limited to substituted and unsubstituted quinolinylmethylamino groups and the like, such as, but not
- limited to alkoxyquinolinylmethylamino groups and the like, such as, but not limited to substituted and unsubstituted 4-alkoxy-2-quinolinylmethylamino groups and the like, and furanylalkylamino groups, and the like. In other embodiments of the fourth group of compounds, R³ is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and unsubstituted
- benzimidazolylalkylamino groups, substituted and unsubstituted imidazolylalkylamino groups, substituted and unsubstituted furanylalkylamino groups, and substituted and unsubstituted arylalkylamino groups. In some such embodiments, R³ is selected from the group consisting of (2-thiazolyl)alkylamino groups, 1-(3-methylbenzimidazolyl)alkylamino groups, 4-(2-
- 30 phenylimidazolyl)alkylamino groups, 4-(2-ethyl-5-methylimidazolyl)alkylamino

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groups, (2-furanyl)alkylamino groups, phenylalkylamino groups, and 1-(2-fluoro-5-alkoxyphenyl)alkylamino groups. In still other such embodiments, R³ is selected from the group consisting of -N(H)-CH₂-(2-thiazolyl) groups, -N(H)-CH₂-(1-(3-methylbenzimidazolyl)) groups, -N(H)-CH₂-(4-(2-phenylimidazolyl)) groups, -N(H)-CH₂-(4-(2-ethyl-5-methylimidazolyl)) groups, -N(H)-CH₂-(2-furanyl) 5 groups, -N(H)-CH₂-phenyl groups, and -N(H)-CH₂-(1-(2-fluoro-5-alkoxyphenyl)) groups. In still another embodiment, R¹ is selected from the group consisting of unsubstituted -NH₂ groups, and substituted and unsubstituted pyrrolidinylalkylamino groups; R² is selected from the group consisting of substituted and unsubstituted 10 thiazolylalkylamino groups, substituted and unsubstituted pyrrolidinylalkylamino groups, and substituted and unsubstituted aminoalkylamino groups; and/or R³ is selected from the group consisting of substituted and unsubstituted thiazolylalkylamino groups, substituted and unsubstituted benzimidazolylalkylamino groups, substituted and unsubstituted imidazolylalkylamino groups, substituted and 15 unsubstituted furanylalkylamino groups, and substituted and unsubstituted arylalkylamino groups. In such compounds, Z¹-Z⁴, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, and R¹⁰ can have any of the other values described in any of the other embodiments of any of the groups of compounds.

In another embodiment of the fourth group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -F.

In another embodiment of the fourth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -Cl.

In another embodiment of the fourth group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -OMe.

In another embodiment of the fourth group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is a substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups where the heterocyclyl group

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of the -C(=O)N(H)-alkyl-heterocyclyl groups is selected from the group consisting of morpholinyl, piperazinyl, and piperidinyl groups.

In another embodiment of the fourth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is H. In some such embodiments, R^8 is also H.

In another embodiment of the fourth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is -CH₃.

In another embodiment of the fourth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is morpholine.

In another embodiment of the fourth group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is H.

In another embodiment of the fourth group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is -CH₃.

In another embodiment of the fourth group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is morpholine.

In another embodiment of the fourth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from a first group; or Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from the first group, the first group comprising members selected from the group consisting of -Br, -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted and unsubstituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted cycloalkylheterocyclyl groups, substituted and unsubstituted heterocyclyloxy groups,

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substituted and unsubstituted aryloxy groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted and unsubstituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups. In some such embodiments, R³ is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C=N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkoxy groups, and substituted alkyl groups, substituted and unsubstituted alkoxy groups, and substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the fourth group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and 15 R⁶ is selected from -Br, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted 20 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted 25 and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted 30

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heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other embodiments, R⁶ has the values described in the preceding sentence and R⁷ is -H.

In another embodiment of the fourth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R^6 is a methoxy group. In still other embodiments of the fourth group of compounds where R^6 is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R^7 is -H.

In another embodiment of the fourth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R⁶ is a methyl group. In still other embodiments of the fourth group of compounds where R⁶ is an alkyl group having from 1-6 carbon atoms such as a methyl group, R⁷ is -H.

In another embodiment of the fourth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted alkoxy group having the formula –OCH₂(CH₂)_mR¹¹ where m is an integer selected from 0, 1, or 2 and R¹¹ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In still other such embodiments, R¹¹ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹¹ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments where R⁶ is a substituted alkoxy group having the formula –OCH₂(CH₂)_mR¹¹, R⁷ is –H. In still other embodiments, R⁶ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, but not

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limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3-pyridinyl)methoxy groups, or the like.

In another embodiment of the fourth group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted amino group having the formula -N(R¹²)(CH₂)_pR¹³ where p is an integer selected from 0, 1, 2, or 3, R¹³ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H or substituted and unsubstituted alkyl groups such as, but not 10 limited to, methyl, ethyl, propyl, and isopropyl. In some such embodiments. R¹³ is selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R¹² is a CH₃ group. In still other such 15 embodiments, R¹³ is selected from substituted alkoxy groups. In still other such embodiments, R¹³ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some 20 embodiments, R⁶ is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1methylpiperidinyl)) groups, -N(H)CH2(2-pyridyl) groups, -N(H)CH2(3-pyridyl) groups, -N(H)CH2(4-pyridyl) groups, -N(H)CH2CH2(2-pyridyl) groups, -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups, 25 -N(CH₃)CH₂CH₂(2-pyridyl) groups -N(H)CH₂CH₂(4-piperidinyl) groups, -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, -N(H)CH2CH2CH2(1-(4-methylpiperazinyl)) groups, -N(H)CH2CH2CH2(4morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, -N(H)CH2CH2CH2(1-pyrrolidinyl) groups, -N(CH3)CH2CH2CH2(diethylamino) groups, and the like. 30

In still other embodiments of the fourth group of compounds where R^6 is a substituted amino group having the formula $-N(R^{12})(CH_2)_0R^{13}$, R^7 is -H.

In another embodiment of the fourth group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted amino group having the formula -N(R¹²)(CH₂)₀R¹³ or the formula $-N(R^{12})C(H)(alkyl)((CH_2)_pR^{13})$ where p is an integer selected from 0, 1, 2, or 3, R^{13} is selected from a methyl group, substituted and unsubstituted alkoxy groups. substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)2 groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H; substituted and 10 unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₃ groups and the like; -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(alkyl)₂ groups such as -C(=O)-CH₂-N(alkyl)₂ groups and the like; -C(=O)-alkyl- $N(R^{12a'})(R^{12b'})$ groups such as -C(=O)- CH_2 - $N(alkyl)_2$ groups and 15 the like -C(=O)-alkyl-heterocyclyl groups such as -C(=O)-CH₂-heterocyclyl groups and the like such as -C(=O)-CH₂-(1-piperazinyl) groups and the like; -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{12a'} is selected from -20 H, and substituted and unsubstituted alkyl groups, and R^{12b'} is selected from -H, -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=0)-alkyl-halogen groups.

In another embodiment of the fourth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values defined in the previous embodiments, Z² is C, and R⁶ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the fourth group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl

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groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted pyrazolyl groups. substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups. substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2,5-diazabicyclo[2.2.1] heptane groups, substituted and unsubstituted 1,4-diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1,4-diazabicyclo[4,3,0]nonane group, and substituted or unsubstituted 10 1,4-diazacycloheptane groups. In still other embodiments of the fourth group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy 15 substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the 20 ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted 25 piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl 30 substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl

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group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl substituted piperazinyl group; a -C(=O)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-ethyl or a -C(=0)-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N 10 atom is bonded to \mathbb{Z}^2 , and the like; a $-\mathbb{C}(=0)$ O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=0)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z², and the like; a cycloalkyl substituted piperazinyl 15 group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl 20 substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl 25 group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted 30

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piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a 5 heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as, but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted 10 pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a 15 hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5diazabicyclo[2,2,1]heptane groups; an alkyl substituted 2,5diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 20 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not 25 limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the fourth group of compounds where R⁶ is a substituted or unsubstituted heterocyclyl group, R⁷ is -H.

In another embodiment of the fourth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from substituted and unsubstituted alkyl groups, substituted and

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unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, 5 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=0)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted 10 alkylheterocyclyl groups and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups. 15 and substituted and unsubstituted heterocyclylamino groups. In still other such embodiments, R⁷ has the values described in the preceding sentence and R⁶ is -H.

In another embodiment of the fourth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R⁷ is a methoxy group. In still other embodiments of the fourth group of compounds where R⁷ is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R⁶ is -H.

In another embodiment of the fourth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R⁷ is a methyl group. In still other embodiments of the fourth group of compounds where R⁷ is an alkyl group having from 1-6 carbon atoms such as a methyl group, R⁶ is -H.

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In another embodiment of the fourth group of compounds, Z^1 , Z^2 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴ where n is an integer selected from 0, 1, or 2 and R14 is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and 5 substituted and unsubstituted heterocyclyl groups. In some embodiments, R¹⁴ is selected from substituted alkoxy groups such as, but not limited to methoxy groups. ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹⁴ is selected from substituted and unsubstituted heterocyclyl groups selected from 10 pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments of the fourth group of compounds where R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴, R⁶ is -H. In still other embodiments, R⁷ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, 15 but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3pyridinyl)methoxy groups, or the like.

In another embodiment of the fourth group of compounds, Z^1 , Z^2 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)₉R¹⁶ where q is an 20 integer selected from 0, 1, 2, or 3 and R¹⁶ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹⁵ is -H or a substituted or unsubstituted alkyl groups, such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups. In some such embodiments. R¹⁶ is 25 selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R15 is a CH3 group. In still other such embodiments. R¹⁶ is selected from substituted alkoxy groups. In still other such

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embodiments, R¹⁶ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some embodiments, R⁷ is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1-methylpiperidinyl)) groups, -N(H)CH₂(2-pyridyl) groups, -N(H)CH₂(3-pyridyl) groups, -N(H)CH₂(4-pyridyl) groups, -N(H)CH₂CH₂(4-pyridyl) groups, -N(H)CH₂CH₂(2-pyridyl) groups, -N(H)CH₂CH₂(4-piperidinyl) groups, -N(H)CH₂CH₂(4-morpholinyl) groups, -N(H)CH₂CH₂(1-imidazolyl) groups, -N(H)CH₂CH₂CH₂(1-(4-methylpiperazinyl)) groups, -N(H)CH₂CH₂CH₂(4-morpholinyl) groups, -N(H)CH₂CH₂CH₂(1-imidazolyl) groups, -N(H)CH₂CH₂CH₂(1-pyrrolidinyl) groups, -N(CH₃)CH₂CH₂CH₂(diethylamino)

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groups, and the like.

In still other embodiments of the fourth group of compounds where R⁷ is a substituted amino group having the formula-N(R¹⁵)(CH₂)₄R¹⁶, R⁶ is -H.

In another embodiment of the fourth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^3 is C, and R^7 is a substituted amino group having the formula $-N(R^{15})(CH_2)_qR^{16}$ or the formula $-N(R^{15})C(H)(alkyl)((CH_2)_qR^{16})$ where q is an integer selected from 0, 1, 2, or 3, R^{16} is selected from a methyl group, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, $-N(alkyl)_2$ groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R^{15} is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(alkyl)₂ groups such as -C(=O)-CH₂-N(alkyl)₂ groups and the like; -C(=O)-alkyl-N(R^{15a})(R^{15b}) groups such as -C(=O)-CH₂-N(alkyl)₂ groups and the like; -C(=O)-alkyl-N(R^{15a})(R^{15b}) groups such as -C(=O)-CH₂-N(alkyl)₂ groups and

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the like -C(=0)-alkyl-heterocyclyl groups such as -C(=0)-CH₂-heterocyclyl groups and the like such as -C(=O)-CH₂-(1-piperazinyl) groups and the like; -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{15a} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{15b'} is selected from -H. -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=O)-alkyl-halogen groups.

In another embodiment of the fourth group of compounds, Z^1 , Z^2 , Z^4 . 10 R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the fourth group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted pyrazolyl groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted imidazolyl groups. substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1,4diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4diazacycloheptane groups. In still other embodiments of the fourth group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as. but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group

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including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl 5 group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3.5-dimethyl substituted piperazinyl group 10 and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted 15 piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl 20 substituted piperazinyl group; a -C(=O)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-ethyl or a -C(=0)-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to \mathbb{Z}^3 , and the like; a $-\mathbb{C}(=0)$ O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted

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piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as, but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group:

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substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2.5-diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4-diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4-diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the fourth group of compounds where R7 is a substituted 10 or unsubstituted heterocyclyl group, R⁶ is -H.

In another embodiment of the fourth group of compounds, Z¹-Z⁴, R¹, R², and R³ have any of the values in previous embodiments, and one of R⁶ or R⁷ is a substituted or unsubstituted pyridyloxy group. In some such embodiments, one of R⁶ or R⁷ is substituted or unsubstituted 2-pyridyloxy group, a 3-pyridyloxy group. or a 4-pyridyloxy group. In other such embodiments, one of R⁶ or R⁷ is a (2-Nalkylamido-4-pyridyl)oxy group such as a (2-N-methylamido-4-pyridyl)oxy group or the like; or a (5-N-alkylamido-3-pyridyl)oxy group such as a (5-N-methylamido-3pyridyl)oxy group, or the like.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a fifth group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl 25 groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-arvl

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groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 5 groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 10 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-15 heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl 20 groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-25 C(=O)-alkyl-heterocyclyl groups;

 R^2 is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, substituted and unsubstituted and unsubstituted and

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unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=0)-alkyl groups, substituted and 5 unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=0)N(H)-aryl groups, substituted and unsubstituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, 10 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, 15 substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 20 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl 25 groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl groups, substituted and 30

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unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R^2 and R^3 are a group of formula -OCH₂O-such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms;

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R³ is selected from -F, -Cl, -Br, -C=N, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted saturated heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF³ groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups;

R⁴ is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted and unsubstitute

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unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-5 C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted 10 heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-15 C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^5 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^5 is absent if Z^1 is N:

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R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and

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substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted heterocyclylamino groups; substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R⁶ is absent if Z² is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁷ is absent if Z³ is N;

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 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R9 is -H; and

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R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups.

In some embodiments, R¹⁰ is -H. In other embodiments, R¹⁰ is an unsubstituted alkyl group having from 1 to 6 carbon atoms such as a methyl, ethyl, propyl, i-propyl group, or the like. In some such embodiments, R¹⁰ is a -CH₃ group.

In one embodiment of the fifth group of compounds, each of Z^1 , Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the fifth group of compounds, Z^1 is N and each of Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the fifth group of compounds, Z^1 and Z^3 are both N and Z^2 and Z^4 are both C.

In another embodiment of the fifth group of compounds, Z^3 is N and 20 each of Z^1 , Z^2 , and Z^4 are C.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 have any of the values in previous embodiments, and R^1 is selected from -H, -F, -Cl, and -Br.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 have any of the values in previous embodiments, and R^1 is a substituted and unsubstituted

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heterocyclylamino group. In some such embodiments, R¹ is a substituted and unsubstituted heteroarylamino groups. In some embodiments, R¹ is a substituted and unsubstituted heterocyclylamino group such as, but not limited to, substituted and unsubstituted pyrroldinylalkylamino groups and the like, such as, but not limited to, substituted and unsubstituted pyrrolidinylmethylamino groups and the like.

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In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is selected from -H. -F. -Cl. -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted 10 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted 15 and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is -H.

In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is an unsubstituted alkoxy 25 group having from 1 to 4 carbon atoms.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a -OMe, -OEt, -O-i-Pr, or -OCH₂CH(CH₃)₂ group.

In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹

have any of the values in previous embodiments, and R² is a substituted or unsubstituted arylalkoxy, a substituted or unsubstituted aryloxy group, or a substituted or unsubstituted heterocyclyoxy group.

In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted benzyloxy group, a substituted or unsubstituted phenoxy group, or a substituted or unsubstituted pyridyloxy group.

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In another embodiment of the fifth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is an unsubstituted alkyl group having from 1 to 4 carbon atoms.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a methyl group.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted -N(H)C(=O)-N(H)-alkyl-aryl group.

In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of substituted and unsubstituted alkylamino groups, dialkylamino groups, cycloalkylamino groups, heterocyclylamino groups, arylalkylamino groups, arylalkylamino groups, arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups. In some embodiments, the substituted and unsubstituted alkylamino groups are substituted and unsubstituted as but not limited to,

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dialkylaminoalkylamino and the like. In some such embodiments the substituted and unsubstituted heterocyclylalkylamino groups are substituted and unsubstituted heteroarylalkylamino groups. In some embodiments, the heterocyclylalkylamino groups include, but are not limited to, substituted and unsubstituted 5 pyrrolidinylalkylamino groups such as, but not limited to, substituted and unsubstituted pyrrolidinylmethylalkylamino groups and the like; substituted and unsubstituted thiazolylalkylamino groups such as, but not limited to substituted and unsubstituted thiazolylmethylamino groups and the like; substituted and unsubstituted imidazolylalkylamino groups such as, but not limited to, 10 imidazolylmethylamino groups and the like; substituted and unsubstituted furanylalkylamino groups such as, but not limited to, substituted and unsubstituted furanylmethylamino groups, and the like; and the like. In other such embodiments, the heterocyclylamino groups are substituted and unsubstituted heteroarylamino groups. In other such embodiments, the substituted and unsubstituted heterocyclylamino groups are substituted and unsubstituted 15 arylalkylheterocyclylamino groups.

In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of isopropylamino groups, 3-(N,N-dimethylamino)propylamino groups, pyrrolidinylmethylamino groups, arylmethylamino groups, arylalkoxyarylmethylamino groups, aryloxyarylmethylamino groups, and pyridylmethylamino groups, and pyridylamino groups.

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In another embodiment of the fifth group of compounds, Z¹-Z⁴ and R¹

25 have any of the values in previous embodiments, and R² is a substituted or unsubstituted heterocyclyl groups. In some such embodiments R² is a substituted or unsubstituted benzimidazolyl group or is a substituted or unsubstituted pyrazolyl group.

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In another embodiment of the fifth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the fifth group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is selected from -F, -Cl, and -OMe.

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In another embodiment of the fifth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)CH₂CH₃ group, a substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted -N(H)C(=O)N(H)C(CH₃)₃ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group, or the like.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 , R^1 , 20 and R^2 have any of the values in previous embodiments, and R^3 is -F.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -Cl.

In another embodiment of the fifth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -OMe.

In some embodiments of the fifth group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and at least one of R⁶ or R⁷ is selected from the group consisting of -CO₂H, substituted and unsubstituted

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heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted cycloalkylheterocyclyl groups, substituted and 5 unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted -N(H)alkyl groups, substituted and unsubstituted -N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted -N(H)-alkyl-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups. substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)-10 heterocyclyl groups. In some such embodiments, at least one of R⁶ or R⁷ is selected from the group consisting of -CO₂H, substituted and unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups. substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted 15 -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)heterocyclyl groups. In another embodiments of the fifth group of compounds, at least one of R⁶ or R⁷ is selected from the group consisting of substituted and unsubstituted piperidinyl substituted heterocyclyl groups, substituted and unsubstituted heterocyclyl substituted piperidinyl groups, substituted and 20 unsubstituted hydroxymethyl substituted piperidinyl groups, dimethylaminoalkyl substituted pyrrolidinyl groups, substituted and unsubstituted 3-alkyl substituted piperazinyl groups, substituted and unsubstituted 3,5-dialkyl substituted piperazinyl groups, substituted and unsubstituted N-hydroxyalkyl substituted piperazinyl groups, substituted and unsubstituted N-alkyl substituted 1,4-diazacycloheptyl groups, 25 substituted and unsubstituted N-ethylpiperazinyl groups, substituted and unsubstituted N-isopropylpiperazinyl groups, substituted and unsubstituted N-sec-butylpiperazinyl groups, unsubstituted piperazinyl groups, substituted and unsubstituted N-2-pyridyl substituted piperazinyl groups, substituted and unsubstituted N-3-pyridyl substituted piperazinyl groups, substituted and unsubstituted N-4-pyridyl substituted piperazinyl groups, substituted and 30

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unsubstituted N(H)-CH₂-pyridyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted 3-alkyl substituted morpholinyl groups, substituted and unsubstituted 3,5-dialkyl substituted morpholinyl groups, dialkylamino substituted pyrrolidinyl 5 groups, pyrrolidinyl groups substituted with both dialkylamino and alkyl groups. substituted and unsubstituted 4-hydroxy substituted piperidinyl groups, substituted and unsubstituted 4-aryl substituted piperidinyl groups, substituted and unsubstituted 4-hydroxy-4-phenyl substituted piperidinyl groups, substituted and unsubstituted cyclohexylpiperazinyl groups, substituted and unsubstituted cyclopentylpiperazinyl 10 groups, substituted and unsubstituted N-alkyl substituted diazabicycloalkane groups. substituted and unsubstituted -N(CH3)(N-alkyl(4-piperidinyl)) groups, substituted and unsubstituted piperazinyl groups further substituted with a -C(=O)-alkyl group on one of the N atoms of the piperazinvl group, substituted and unsubstituted -N(H)CH₂CH₂-imidazolyl groups, substituted and unsubstituted 15 -N(H)CH2CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2CH2-morpholinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH2CH2-pyridyl groups, substituted and unsubstituted -N(H)CH2CH2-20 imidazolyl groups, substituted and unsubstituted -N(H)CH₂CH₂-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2-morpholinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH2CH2pyridyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, and 25 substituted and unsubstituted 1,4-diazacycloheptane groups. In other embodiments, at least one of R⁶ or R⁷ is selected from the group consisting of piperidinyl substituted piperidinyl groups such as 4-piperidinylpiperidinyl groups or the like, 4-hydroxymethylpiperidinyl groups, 3-dimethylaminomethylpyrrolidinyl groups, 3alkyl substituted piperazinyl groups, 3,5-dialkyl substituted piperazinyl groups, N-

hydroxyethylpiperazinyl groups, N-hydroxymethylpiperazinyl groups, N-

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hydroxypropylpiperazinyl groups, N-methyl substituted 1,4-diazacycloheptyl groups, N-ethylpiperazinyl groups, N-isopropylpiperazinyl groups, N-secbutylpiperazinyl groups, unsubstituted piperazinyl groups, N-(2-pyridyl)piperazinyl groups, N-(3-pyridyl)piperazinyl groups, N-(4-pyridyl)piperazinyl groups,

- 5 N(H)-CH₂-pyridyl groups, imidazolyl groups, unsubstituted morpholinyl groups, 3-alkylmorpholinyl groups, 3,5-dialkylmorpholinyl groups,
 - 2-dimethylaminopyrrolidinyl groups, 2-methyl-4-dialkylaminopyrroldinyl groups,
 - 4-hydroxypiperidinyl groups, 4-arylpiperidinyl groups,
 - 4-hydroxy-4-phenylpiperidinyl groups, cyclohexylpiperazinyl groups,
- 10 cyclopentylpiperazinyl groups, N-methyl substituted diazabicycloalkane groups,
 - -N(CH₃)(N-alkyl(4-piperidinyl)) groups, piperazinyl groups further substituted with
 - a -C(=0)-methyl group on one of the N atoms of the piperazinyl group,
 - -N(H)CH2CH2CH2-imidazolyl groups, -N(H)CH2CH2-pyrrolidinyl groups,
 - -N(H)CH2CH2CH2-morpholinyl groups, -N(H)CH2CH2CH2-piperazinyl groups,
- -N(H)CH2CH2CH2-piperidinyl groups, and -N(H)CH2CH2CH2-pyridyl groups. In some such embodiments, at least one of R⁶ or R⁷ is selected from the group consisting of 4-piperidinylpiperidinyl groups, 4-hydroxymethylpiperidinyl groups, 3-dimethylaminomethylpyrrolidinyl groups, 3,5-dimethyl substituted piperazinyl groups, N-methyl substituted 1,4-diazacycloheptyl groups, N-(2-pyridyl)piperazinyl
- groups, N(H)-CH₂-(4-pyridyl) groups, imidazolyl groups, unsubstituted morpholinyl groups, 3-methylmorpholinyl groups, 3,5-dimethylmorpholinyl groups,
 - 2-dimethylaminopyrrolidinyl groups, 2-methyl-4-dimethylaminopyrroldinyl groups,
 - 4-hydroxy-4-phenylpiperidinyl groups, cyclohexylpiperazinyl groups, N-methyl
 - substituted diazabicycloalkane groups, -N(CH3)(N-methyl(4-piperidinyl)) groups,
- piperazinyl groups further substituted with a -C(=O)-methyl group on one of the N atoms of the piperazinyl group, -N(H)CH₂CH₂-imidazolyl groups,
 - -N(H)CH2CH2-pyrrolidinyl groups, -N(H)CH2CH2-morpholinyl groups,
 - -N(H)CH2CH2CH2-piperazinyl groups, -N(H)CH2CH2-Piperidinyl groups, and
 - -N(H)CH2CH2CH2-pyridyl groups.

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In another embodiment of the fifth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is H. In some such embodiments, R^8 is also H.

In another embodiment of the fifth group of compounds, Z^2-Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is -CH₃.

In another embodiment of the fifth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is morpholine.

In another embodiment of the fifth group of compounds, Z^1-Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is H.

In another embodiment of the fifth group of compounds, Z^1-Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is -CH₃.

In another embodiment of the fifth group of compounds, Z¹-Z³, R¹, R², and R³ have any of the values in previous embodiments, Z⁴ is C, and R⁸ is morpholine.

In another embodiment of the fifth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from a first group of compounds; or Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from the first group of compounds comprising members selected from the group consisting of -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted and unsubstituted heterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted and unsubstituted

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heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, -C(=O)N(H)-heteroaryl groups, substituted and unsubstituted -C(=O)N(alkyl) (heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups.

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In another embodiment of the fifth group of compounds, Z¹, Z³, Z⁴, R¹. R². R³. R⁵. and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from -Br, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted 10 heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted 15 -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and 20 unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other embodiments, R⁶ has the values described in the preceding sentence and R⁷ is -H. 25

In another embodiment of the fifth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R^6 is a methoxy group. In still other embodiments of the fifth group

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of compounds where R^6 is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R^7 is -H.

In another embodiment of the fifth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R^6 is a methyl group. In still other embodiments of the fifth group of compounds where R^6 is an alkyl group having from 1-6 carbon atoms such as a methyl group, R^7 is -H.

In another embodiment of the fifth group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and 10 R⁶ is a substituted alkoxy group having the formula -OCH₂(CH₂)_mR¹¹ where m is an integer selected from 0, 1, or 2 and R11 is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In still other such embodiments, 15 R¹¹ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹¹ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments where R⁶ is a substituted alkoxy group having the formula -OCH₂(CH₂)_mR¹¹, R⁷ is -H. In still other 20 embodiments, R⁶ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3-pyridinyl)methoxy groups, or the like. 25

In another embodiment of the fifth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is a substituted amino group having the formula $-N(R^{12})(CH_2)_pR^{13}$ where p is an integer selected from 0, 1, 2, or 3, R^{13} is selected from substituted and unsubstituted

alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H or substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl. In some such embodiments, R¹³ is 5 selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R¹² is a CH₃ group. In still other such embodiments, R¹³ is selected from substituted alkoxy groups. In still other such embodiments, R¹³ is selected from substituted and unsubstituted heterocyclyl groups 10 such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some embodiments, R⁶ is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1-15 methylpiperidinyl)) groups, -N(H)CH₂(2-pyridyl) groups, -N(H)CH₂(3-pyridyl) groups, -N(H)CH2(4-pyridyl) groups, -N(H)CH2CH2(2-pyridyl) groups, -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups, -N(CH₃)CH₂CH₂(2-pyridyl) groups -N(H)CH₂CH₂(4-piperidinyl) groups. -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, 20 -N(H)CH2CH2CH2(1-(4-methylpiperazinyl)) groups, -N(H)CH2CH2CH2(4morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, -N(H)CH2CH2CH2(1-pyrrolidinyl) groups, -N(CH3)CH2CH2CH2(diethylamino) groups, and the like.

In still other embodiments of the fifth group of compounds where R^6 is a substituted amino group having the formula $-N(R^{12})(CH_2)_pR^{13}$, R^7 is -H.

In another embodiment of the fifth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is a substituted amino group having the formula $-N(R^{12})(CH_2)_pR^{13}$ or the formula $-N(R^{12})C(H)(alkyl)((CH_2)_pR^{13})$ where p is an integer selected from 0, 1, 2, or 3, R^{13}

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is selected from a methyl group, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)₂ groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₃ groups and the like; -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(alkyl)2 groups such as -C(=O)-CH2-N(alkyl)2 groups and the like; -C(=O)-alkyl- $N(R^{12a})(R^{12b})$ groups such as -C(=O)-CH₂- $N(alkyl)_2$ groups and 10 the like -C(=O)-alkyl-heterocyclyl groups such as -C(=O)-CH₂-heterocyclyl groups and the like such as $-C(=O)-CH_2-(1-piperazinyl)$ groups and the like: -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH2-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=0)-CH₂-S-alkyl groups and the like; and the like where R^{12a'} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{12b'} is selected from -H, 15 -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=O)-alkyl-halogen groups.

In another embodiment of the fifth group of compounds, Z¹, Z³, Z⁴,

R¹, R², R³, R⁵, and R⁸ have any of the values defined in the previous embodiments,

Z² is C, and R⁶ is a substituted or unsubstituted heterocyclyl group. In some
embodiments of the fifth group of compounds where R⁶ is a heterocyclyl group, the
heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups,
substituted and unsubstituted pyridyl groups, substituted and unsubstituted

morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted
and unsubstituted piperidinyl groups, substituted and unsubstituted pyrazolyl groups,
substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted
imidazolyl groups, substituted and unsubstituted 1,4-diazacycloheptane groups,
substituted and unsubstituted 2,5-diazabicyclo[2.2.1]heptane groups, substituted and
unsubstituted 1,4-diazabicyclo[2.2.2]octane groups, substituted or unsubstituted

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1,4-diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4-diazacycloheptane groups. In still other embodiments of the fifth group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, 5 but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited 10 to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl 15 substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, 20 but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl 25 substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl substituted piperazinyl group; a -C(=O)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=O)-ethyl or a -C(=O)-methyl substituted piperazinyl 30

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group, and the like such as a piperazinyl group where the -C(=0)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to \mathbb{Z}^2 , and the like; a $-\mathbb{C}(=0)$ O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted 5 piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z², and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted 10 piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy 15 substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited 20 to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and 25 the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as, but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not 30

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limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2,5diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1.4diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the fifth group of compounds where R⁶ is a substituted or unsubstituted heterocyclyl group, R⁷ is -H.

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In another embodiment of the fifth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclyl groups, substituted

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and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted and unsubstituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other such embodiments, R⁷ has the values described in the preceding sentence and R⁶ is -H.

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In another embodiment of the fifth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R⁷ is a methoxy group. In still other embodiments of the fifth group of compounds where R⁷ is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R⁶ is -H.

In another embodiment of the fifth group of compounds, Z^1 , Z^2 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^3 is C, and R^7 is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R^7 is a methyl group. In still other embodiments of the fifth group of compounds where R^7 is an alkyl group having from 1-6 carbon atoms such as a methyl group, R^6 is -H.

In another embodiment of the fifth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴ where n is an integer selected from 0, 1, or 2 and R¹⁴ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In some embodiments, R¹⁴ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹⁴ is

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selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments of the fifth group of compounds where R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴, R⁶ is -H. In still other embodiments, R⁷ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3-pyridinyl)methoxy groups, or the like.

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10 In another embodiment of the fifth group of compounds, Z^1 , Z^2 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)_qR¹⁶ where q is an integer selected from 0, 1, 2, or 3 and R¹⁶ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. 15 and R15 is -H or a substituted or unsubstituted alkyl groups, such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups. In some such embodiments, R¹⁶ is selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, 20 (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R15 is a CH3 group. In still other such embodiments, R¹⁶ is selected from substituted alkoxy groups. In still other such embodiments, R¹⁶ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, 25 morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some embodiments, R^7 is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1methylpiperidinyl)) groups, -N(H)CH₂(2-pyridyl) groups, -N(H)CH₂(3-pyridyl) groups, -N(H)CH2(4-pyridyl) groups, -N(H)CH2CH2(2-pyridyl) groups, -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups, 30

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- -N(CH₃)CH₂CH₂(2-pyridyl) groups -N(H)CH₂CH₂(4-piperidinyl) groups,
- -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups,
- -N(H)CH₂CH₂(1-(4-methylpiperazinyl)) groups, -N(H)CH₂CH₂(4-morpholinyl) groups, -N(H)CH₂CH₂(1-imidazolyl) groups,
- 5 -N(H)CH₂CH₂CH₂(1-pyrrolidinyl) groups, -N(CH₃)CH₂CH₂CH₂(diethylamino) groups, and the like.

In still other embodiments of the fifth group of compounds where R^7 is a substituted amino group having the formula- $N(R^{15})(CH_2)_qR^{16}$, R^6 is -H.

In another embodiment of the fifth group of compounds, Z^1 , Z^3 , Z^4 , 10 R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)₉R¹⁶ or the formula $-N(R^{15})C(H)(alkyl)((CH₂)₀R^{16})$ where q is an integer selected from 0, 1, 2, or 3, R^{16} is selected from a methyl group, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)₂ groups and the like, substituted and unsubstituted aryl groups, and substituted and 15 unsubstituted heterocyclyl groups, and R¹⁵ is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₃ groups and the like; -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(alkyl)₂ groups such as -C(=O)-CH₂-N(alkyl)₂ groups and the 20 like; -C(=O)-alkyl- $N(R^{15a'})(R^{15b'})$ groups such as -C(=O)-CH₂- $N(alkyl)_2$ groups and the like -C(=0)-alkyl-heterocyclyl groups such as -C(=0)-CH₂-heterocyclyl groups and the like such as -C(=O)-CH₂-(1-piperazinyl) groups and the like; -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as 25 -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{15a'} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{15b} is selected from -H, -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2-

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pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=O)-alkyl-halogen groups.

In another embodiment of the fifth group of compounds, Z^1 , Z^2 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the 5 fifth group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted 10 piperidinyl groups, substituted and unsubstituted pyrazolyl groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted imidazolyl groups, and substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4-15 diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1,4diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4diazacycloheptane groups. In still other embodiments of the fifth group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as. 20 but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but 25 not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl 30

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substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, 5 but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl 10 substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=O)O-alkyl substituted piperazinyl group; a -C(=0)-alkyl substituted piperazinyl group such as. but not limited to, a -C(=O)-ethyl or a -C(=O)-methyl substituted piperazinyl 15 group, and the like such as a piperazinyl group where the -C(=O)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a -C(=0)O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted 20 piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted 25 piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl 30

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groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited 5 to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and 10 the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as, but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not 15 limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the 20 like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5-25 diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2,5-diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4-diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4-diazacycloheptane group and the like, such as, but not limited to, an 30

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N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the fifth group of compounds where R⁷ is a substituted or unsubstituted heterocyclyl group, R⁶ is -H.

In another embodiment of the fifth group of compounds, Z¹-Z⁴, R¹, R², and R³ have any of the values in previous embodiments, and one of R⁶ or Rⁿ is a substituted or unsubstituted pyridyloxy group. In some such embodiments, one of R⁶ or Rⁿ is substituted or unsubstituted 2-pyridyloxy group, a 3-pyridyloxy group, or a 4-pyridyloxy group. In other such embodiments, one of R⁶ or Rⁿ is a (2-N-alkylamido-4-pyridyl)oxy group such as a (2-N-methylamido-4-pyridyl)oxy group or the like; or a (5-N-alkylamido-3-pyridyl)oxy group such as a (5-N-methylamido-3-pyridyl)oxy group, or the like.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a sixth group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

R¹ is selected from -H, -F, -Cl, -Br, -NO2, -C≡N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO2-alkyl groups, substituted and unsubstituted -N(H)-SO2-aryl groups, -N(H)-SO2-CF3 groups, substituted and unsubstituted -N(H)-SO2-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted and unsubstituted alkoxy groups, substituted and unsubstituted and unsubstituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-

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heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 5 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl 10 groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and 15 unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

R² is selected from -F, -Cl, -Br, -C≡N, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups,

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-N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms;

 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 10 -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups. substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 15 unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted 20 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 25 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 30

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unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=0)-O-alkyl groups, -OH, 10 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=0)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted 15 -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl 20 groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 25 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and 30

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unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted and unsubstituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

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R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

-C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)heterocyclyl groups; or R⁷ is absent if Z³ is N;

R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

R9 is -H: and

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R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups.

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In some embodiments, R^{10} is -H. In other embodiments, R^{10} is an unsubstituted alkyl group having from 1 to 6 carbon atoms such as a methyl, ethyl, propyl, i-propyl group, or the like. In some such embodiments, R^{10} is a -CH₃ group.

In one embodiment of the sixth group of compounds, each of Z^1 , Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the sixth group of compounds, Z^1 is N and each of Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the sixth group of compounds, Z^1 and Z^3 are both N and Z^2 and Z^4 are both C.

In another embodiment of the sixth group of compounds, Z^3 is N and each of Z^1 , Z^2 , and Z^4 are C.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 have any of the values in previous embodiments, and R^1 is selected from -H, -F, -Cl, and -Br.

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In another embodiment of the sixth group of compounds, Z¹-Z⁴ have any of the values in previous embodiments, and R¹ is a substituted and unsubstituted heterocyclylamino group. In some such embodiments, R¹ is a substituted and unsubstituted heteroarylamino groups. In some embodiments, R¹ is a substituted and unsubstituted heterocyclylamino group such as, but not limited to, substituted and unsubstituted pyrroldinylalkylamino groups and the like, such as, but not limited to, substituted and unsubstituted pyrroldinylmethylamino groups and the like.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is an unsubstituted alkoxy group having from 1 to 4 carbon atoms.

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In another embodiment of the sixth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a -OMe, -OEt, -O-i-Pr, or -OCH₂CH(CH₃)₂ group.

In another embodiment of the sixth group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted arylalkoxy, a substituted or unsubstituted aryloxy group, or a substituted or unsubstituted heterocyclyloxy group.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted benzyloxy group, a substituted or unsubstituted phenoxy group, or a substituted or unsubstituted pyridyloxy group.

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In another embodiment of the sixth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted -N(H)C(=O)-N(H)-alkyl-aryl group such as, but not limited to, a -N(H)C(=O)-N(H)-CH₂-aryl group, a -N(H)C(=O)-N(H)-CH₂-aryl group, or the like such as a -N(H)C(=O)-N(H)-CH₂-phenyl group, or the like.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from -H, -F, -Cl, and -OMe.

In another embodiment of the sixth group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -H.

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In another embodiment of the sixth group of compounds, Z^1-Z^4 , R^1 , and R² have any of the values in previous embodiments, and R³ is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C≡N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted -N(H)C(=O)N(H)alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups and substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH2O- such that R2 and R3 define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the sixth group of compounds, Z¹-Z⁴, R¹, 10 and R² have any of the values in previous embodiments, and R³ is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups. and substituted and unsubstituted -N(H)C(=O)N(H)-arvl groups. In some such embodiments, R³ is a substituted or unsubstituted -N(H)C(=O)N(H)CH₂CH₃ group, a substituted or unsubstituted -N(H)C(=O)N(H)CH(CH₃)₂ group, a substituted or unsubstituted -N(H)C(=O)N(H)C(CH₃)₃ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group,

a-N(H)C(=O)N(H)-(trifluoromethylphenyl) group, or the like.

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In another embodiment of the sixth group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is a substituted amino group selected from substituted or unsubstituted arylalkylamino groups such as, but not limited to, phenylalkylamino groups, (halo)(alkoxy)arylalkylamino groups, such as, but not limited to 2-fluoro-5-methoxyphenylmethylamino groups, monoalkoxyarylalkylamino groups, dialkoxyarylalkylamino groups, and the like, such as, but not limited to, 2,5-dialkoxyarylalkylamino groups and the like such as, but not limited to 2,5-dialkoxyarylmethylamino groups, substituted and unsubstituted arylalkoxyarylalkylamino groups such as, but not limited to substituted

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and unsubstituted arylalkoxyarylmethylamino groups and the like, such as, but not limited to, substituted and unsubstituted arylmethoxyarylmethylamino groups and the like, such as, but not limited to substituted and unsubstituted fluoroarylmethoxyarylmethylamino groups and the like, such as, but not limited to, substituted and unsubstituted 4-fluorophenylmethoxyphenyl-methylamino groups and 5 the like; substituted and unsubstituted heterocyclylalkylamino groups including heteroarylalkylamino groups such as, but not limited to substituted and unsubstituted thiazolylalkylamino groups, benzimidazolylalkylamino groups such as, but not limited to N-methylbenzimidazolylalkylamino groups and the like, 10 imidazolylalkylamino groups such as, but not limited to phenylimidazolylalkylamino groups, ethylmethylimidazolylalkylamino groups, and the like, substituted and unsubstituted quinolinylalkylamino groups, such as, but not limited to substituted and unsubstituted quinolinylmethylamino groups and the like, such as, but not limited to alkoxyquinolinylmethylamino groups and the like, such as, but not limited

In another embodiment of the sixth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -F.

to substituted and unsubstituted 4-alkoxy-2-quinolinylmethylamino groups and the

like, and furanylalkylamino groups, and the like.

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In another embodiment of the sixth group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -C1.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -OMe.

In another embodiment of the sixth group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is a substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups where the heterocyclyl group of the -C(=O)N(H)-alkyl-heterocyclyl groups is selected from the group consisting of morpholinyl, piperazinyl, and piperidinyl groups.

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In another embodiment of the sixth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is H. In some such embodiments, R^8 is also H.

In another embodiment of the sixth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is -CH₃.

In another embodiment of the sixth group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is morpholine.

In another embodiment of the sixth group of compounds, Z^1-Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is H.

In another embodiment of the sixth group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is -CH₃.

In another embodiment of the sixth group of compounds, Z¹-Z³, R¹, R², and R³ have any of the values in previous embodiments, Z⁴ is C, and R⁸ is morpholine.

In another embodiment of the sixth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from a first group; or Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is selected from the first group, the first group comprising members selected from the group consisting of -Br, -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted cycloalkylheterocyclyl groups, substituted and unsubstituted end unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted

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heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)heterocyclyl groups, substituted and unsubstituted -C(=0)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups. In some such embodiments, R³ is selected from the group consisting of -F, -Cl, -Br, -CF₃, -C=N, -NO2, -CO2H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, and substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms. In another embodiments of the sixth group of compounds, at least one of Z² or Z³ is C and at least one of R⁶ or R⁷ is selected from the group consisting of substituted and unsubstituted piperidinyl substituted heterocyclyl groups, substituted and unsubstituted heterocyclyl substituted piperidinyl groups, substituted and unsubstituted hydroxymethyl substituted piperidinyl groups, dimethylaminoalkyl substituted pyrrolidinyl groups, substituted and unsubstituted 3-alkyl substituted piperazinyl groups, substituted and unsubstituted 3,5-dialkyl substituted piperazinyl groups, substituted and unsubstituted N-hydroxyalkyl substituted piperazinyl groups, substituted and unsubstituted N-alkyl substituted 1,4-diazacycloheptyl groups, substituted and unsubstituted N-ethylpiperazinyl groups, substituted and unsubstituted N-isopropylpiperazinyl groups, substituted and unsubstituted N-sec-butylpiperazinyl groups, unsubstituted piperazinyl groups, substituted and unsubstituted N-2-pyridyl substituted piperazinyl groups, substituted and unsubstituted N-3-pyridyl substituted piperazinyl groups, substituted and unsubstituted N-4-pyridyl substituted piperazinyl groups, substituted and unsubstituted N(H)-CH2-pyridyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted 3-alkyl substituted morpholinyl groups, substituted and unsubstituted 3,5-dialkyl substituted morpholinyl groups, dialkylamino substituted pyrrolidinyl groups, pyrrolidinyl groups substituted with both dialkylamino and

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alkyl groups, substituted and unsubstituted 4-hydroxy substituted piperidinyl groups. substituted and unsubstituted 4-aryl substituted piperidinyl groups, substituted and unsubstituted 4-hydroxy-4-phenyl substituted piperidinyl groups, substituted and unsubstituted cyclohexylpiperazinyl groups, substituted and unsubstituted cyclopentylpiperazinyl groups, substituted and unsubstituted N-alkyl substituted diazabicycloalkane groups, substituted and unsubstituted -N(CH₃)(N-alkyl(4piperidinyl)) groups, substituted and unsubstituted piperazinyl groups further substituted with a -C(=O)-alkyl group on one of the N atoms of the piperazinyl group, substituted and unsubstituted -N(H)CH2CH2CH2-imidazolyl groups, substituted and unsubstituted -N(H)CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2-morpholinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH₂CH₂-pyridyl groups, substituted and unsubstituted -N(H)CH₂CH₂imidazolyl groups, substituted and unsubstituted -N(H)CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2-morpholinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH2CH2pyridyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, and substituted and unsubstituted 1,4-diazacycloheptane groups. In other embodiments, at least one of R⁶ or R⁷ is selected from the group consisting of piperidinyl substituted piperidinyl groups such as 4-piperidinylpiperidinyl groups or the like, 4-hydroxymethylpiperidinyl groups, 3-dimethylaminomethylpyrrolidinyl groups, 3alkyl substituted piperazinyl groups, 3,5-dialkyl substituted piperazinyl groups, Nhydroxyethylpiperazinyl groups, N-hydroxymethylpiperazinyl groups, Nhydroxypropylpiperazinyl groups, N-methyl substituted 1,4-diazacycloheptyl groups, N-ethylpiperazinyl groups, N-isopropylpiperazinyl groups, N-secbutylpiperazinyl groups, unsubstituted piperazinyl groups, N-(2-pyridyl)piperazinyl groups, N-(3-pyridyl)piperazinyl groups, N-(4-pyridyl)piperazinyl groups,

N(H)-CH₂-pyridyl groups, imidazolyl groups, unsubstituted morpholinyl groups, 3-

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alkylmorpholinyl groups, 3,5-dialkylmorpholinyl groups,

2-dimethylaminopyrrolidinyl groups, 2-methyl-4-dialkylaminopyrroldinyl groups,

- 4-hydroxypiperidinyl groups, 4-arylpiperidinyl groups,
- 4-hydroxy-4-phenylpiperidinyl groups, cyclohexylpiperazinyl groups,
- 5 cyclopentylpiperazinyl groups, N-methyl substituted diazabicycloalkane groups,
- -N(CH₃)(N-alkyl(4-piperidinyl)) groups, piperazinyl groups further substituted with
 - a -C(=O)-methyl group on one of the N atoms of the piperazinyl group,
 - -N(H)CH2CH2CH2-imidazolyl groups, -N(H)CH2CH2CH2-pyrrolidinyl groups,
 - -N(H)CH2CH2CH2-morpholinyl groups, -N(H)CH2CH2-piperazinyl groups,
- -N(H)CH₂CH₂-piperidinyl groups, and -N(H)CH₂CH₂-pyridyl groups. In some such embodiments, at least one of R⁶ or R⁷ is selected from the group consisting of 4-piperidinylpiperidinyl groups, 4-hydroxymethylpiperidinyl groups, 3-dimethylaminomethylpyrrolidinyl groups, 3,5-dimethyl substituted piperazinyl groups, N-methyl substituted 1,4-diazacycloheptyl groups, N-(2-pyridyl)piperazinyl
- groups, N(H)-CH₂-(4-pyridyl) groups, imidazolyl groups, unsubstituted morpholinyl groups, 3-methylmorpholinyl groups, 3,5-dimethylmorpholinyl groups,
 - 2-dimethylaminopyrrolidinyl groups, 2-methyl-4-dimethylaminopyrroldinyl groups,
 - 4-hydroxy-4-phenylpiperidinyl groups, cyclohexylpiperazinyl groups, N-methyl
 - $substituted\ diazabicycloalkane\ groups,\ -N(CH_3)(N-methyl(4-piperidinyl))\ groups,$
- piperazinyl groups further substituted with a -C(=O)-methyl group on one of the N atoms of the piperazinyl group, -N(H)CH₂CH₂-imidazolyl groups,
 - $-N(H)CH_2CH_2CH_2-pyrrolidinyl\ groups,\ -N(H)CH_2CH_2CH_2-morpholinyl\ groups,$
 - $-N(H)CH_2CH_2-piperazinyl\ groups,\ -N(H)CH_2CH_2-piperidinyl\ groups,\ and$
 - -N(H)CH2CH2CH2-pyridyl groups.
- In another embodiment of the sixth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is selected from -Br, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted

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-C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted and unsubstituted and unsubstituted and unsubstituted heterocyclylamino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted and unsubstituted

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In another embodiment of the sixth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R⁶ is a methoxy group. In still other embodiments of the sixth group of compounds where R⁶ is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R⁷ is -H.

In another embodiment of the sixth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R^6 is a methyl group. In still other embodiments of the sixth group of compounds where R^6 is an alkyl group having from 1-6 carbon atoms such as a methyl group, R^7 is -H.

In another embodiment of the sixth group of compounds, Z^1 , Z^3 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^2 is C, and R^6 is a substituted alkoxy group having the formula $-OCH_2(CH_2)_mR^{11}$ where m is an

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integer selected from 0, 1, or 2 and R¹¹ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In still other such embodiments, R¹¹ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹¹ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments where R⁶ is a substituted alkoxy group having the formula –OCH₂(CH₂)_mR¹¹, R⁷ is –H. In still other embodiments, R⁶ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as, but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3-pyridinyl)methoxy groups, or the like.

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In another embodiment of the sixth group of compounds, Z^1 , Z^3 , Z^4 , 15 R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and R⁶ is a substituted amino group having the formula $-N(R^{12})(CH_2)_pR^{13}$ where p is an integer selected from 0, 1, 2, or 3, R¹³ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and 20 unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H or substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl. In some such embodiments, R¹³ is selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, 25 (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R¹² is a CH₃ group. In still other such embodiments, R¹³ is selected from substituted alkoxy groups. In still other such embodiments, R¹³ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some 30

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embodiments, R^6 is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1-methylpiperidinyl)) groups, -N(H)CH₂(2-pyridyl) groups, -N(H)CH₂(3-pyridyl) groups, -N(H)CH₂(4-pyridyl) groups, -N(H)CH₂(2-pyridyl) groups,

- -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups,
 -N(CH3)CH2CH2(2-pyridyl) groups -N(H)CH2CH2(4-piperidinyl) groups,
 -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2(1-imidazolyl) groups,
 - -N(H)CH₂CH₂CH₂(1-(4-methylpiperazinyl)) groups, -N(H)CH₂CH₂CH₂(4-morpholinyl) groups, -N(H)CH₂CH₂(1-imidazolyl) groups,
- 10 -N(H)CH₂CH₂CH₂(1-pyrrolidinyl) groups, -N(CH₃)CH₂CH₂CH₂(diethylamino) groups, and the like.

In still other embodiments of the sixth group of compounds where R^6 is a substituted amino group having the formula $-N(R^{12})(CH_2)_pR^{13}$, R^7 is -H.

In another embodiment of the sixth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z² is C, and 15 R⁶ is a substituted amino group having the formula -N(R¹²)(CH₂)_pR¹³ or the formula $-N(R^{12})C(H)(alkyl)((CH_2)_pR^{13})$ where p is an integer selected from 0, 1, 2, or 3, R^{13} is selected from a methyl group, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)2 20 groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹² is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₃ groups and the like; -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like; -C(=O)-alkyl-N(alkyl)2 groups such as -C(=O)-CH2-N(alkyl)2 groups and the 25 like; -C(=O)-alkyl-N(R^{12a'})(R^{12b'}) groups such as -C(=O)-CH₂-N(alkyl)₂ groups and the like -C(=O)-alkyl-heterocyclyl groups such as -C(=O)-CH₂-heterocyclyl groups and the like such as $-C(=0)-CH_2-(1-piperazinyl)$ groups and the like; -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups

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such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{12a'} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{12b'} is selected from -H, -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2-pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=O)-alkyl-halogen groups.

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In another embodiment of the sixth group of compounds, Z^1 , Z^3 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values defined in the previous embodiments, Z² is C, and R⁶ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the sixth group of compounds where R⁶ is a heterocyclyl group, the 10 heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted pyrazolyl groups, 15 substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2.5-diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4-diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 20 1,4-diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4-diazacycloheptane groups. In still other embodiments of the sixth group of compounds where R⁶ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy 25 substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the 30

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ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinvl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=0)O-alkyl substituted piperazinyl group; a - C(=0)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=O)-ethyl or a -C(=O)-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=0)-ethyl or the -C(=0)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to \mathbb{Z}^2 , and the like; a $-\mathbb{C}(=0)$ O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=0)-Oethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z², and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl

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substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as. but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2.5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 2,5-

diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted

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2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4-diazacycloheptane group such as, but not limited to, an alkyl substituted 1,4-diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the sixth group of compounds where R⁶ is a substituted or unsubstituted heterocyclyl group, R⁷ is -H.

In another embodiment of the sixth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and 10 R⁷ is selected from substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, 15 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted $-\dot{C}(=0)$ -heterocyclyl groups, substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted 20 and unsubstituted arytheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, and substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and 25 unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups. In still other such embodiments, R⁷ has the values described in the preceding sentence and R⁶ is -H.

In another embodiment of the sixth group of compounds, Z^1 , Z^2 , Z^4 , R^1 , R^2 , R^3 , R^5 , and R^8 have any of the values in previous embodiments, Z^3 is C, and R^7 is an alkoxy group having from 1-6 carbon atoms. In still other such embodiments, R^7 is a methoxy group. In still other embodiments of the sixth group of compounds where R^7 is an alkoxy group having from 1-6 carbon atoms such as a methoxy group, R^6 is -H.

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In another embodiment of the sixth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is an alkyl group having from 1-6 carbon atoms. In still other such embodiments, R⁷ is a methyl group. In still other embodiments of the sixth group of compounds where R⁷ is an alkyl group having from 1-6 carbon atoms such as a methyl group, R⁶ is -H.

In another embodiment of the sixth group of compounds, Z^1 , Z^2 , Z^4 , R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴ where n is an integer selected from 0, 1, or 2 and R14 is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups. In some embodiments, R¹⁴ is selected from substituted alkoxy groups such as, but not limited to methoxy groups, ethoxy groups, propoxy groups, and the like. In still other such embodiments, R¹⁴ is selected from substituted and unsubstituted heterocyclyl groups selected from pyrrolidinyl groups, pyridyl groups, morpholinyl groups, piperazinyl groups, and piperidinyl groups. In still other embodiments of the sixth group of compounds where R⁷ is a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴, R⁶ is -H. In still other embodiments, R⁷ is a pyrrolidinylalkoxy groups, such as but not limited to, a pyrrolidinylpropoxy group or the like; an alkoxyethoxy group such as. but not limited to, a methoxyethoxy group or the like; or a substituted or unsubstituted pyridinylalkoxy group such as, but not limited to, (3pyridinyl)methoxy groups, or the like.

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In another embodiment of the sixth group of compounds, Z^1 , Z^2 , Z^4 . R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)_qR¹⁶ where q is an integer selected from 0, 1, 2, or 3 and R¹⁶ is selected from substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted 5 and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹⁵ is -H or a substituted or unsubstituted alkyl groups, such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups. In some such embodiments. R¹⁶ is selected from substituted amino groups such as alkylamino groups and dialkylamino groups, such as, but not limited to, dimethylamino, diethylamino, dipropylamino, 10 (methyl)(ethyl)amino, (ethyl)(propyl)amino, (methyl)(propyl)amino groups, and the like. In some such embodiments, R15 is a CH3 group. In still other such embodiments, R¹⁶ is selected from substituted alkoxy groups. In still other such embodiments, R¹⁶ is selected from substituted and unsubstituted heterocyclyl groups such as those selected from pyrrolidinyl groups, pyrazolyl groups, pyridyl groups, 15 morpholinyl groups, piperazinyl groups, piperidinyl groups, and the like. In some embodiments, R^7 is selected from -N(H)(3-piperidinyl) groups, -N(H)(4-piperidinyl) groups, -N(H)(4-(2-methoxymethylpyrrolidinyl)) groups, -N(CH₃)(4-(1methylpiperidinyl)) groups, -N(H)CH₂(2-pyridyl) groups, -N(H)CH₂(3-pyridyl) groups, -N(H)CH2(4-pyridyl) groups, -N(H)CH2CH2(2-pyridyl) groups, 20 -N(H)CH2CH2(3-pyridyl) groups, -N(H)CH2CH2(4-pyridyl) groups, -N(CH₃)CH₂CH₂(2-pyridyl) groups -N(H)CH₂CH₂(4-piperidinyl) groups, -N(H)CH2CH2(4-morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, -N(H)CH2CH2CH2(1-(4-methylpiperazinyl)) groups, -N(H)CH2CH2CH2(4-25 morpholinyl) groups, -N(H)CH2CH2CH2(1-imidazolyl) groups, -N(H)CH2CH2CH2(1-pyrrolidinyl) groups, -N(CH3)CH2CH2CH2(diethylamino) groups, and the like.

In still other embodiments of the sixth group of compounds where R^7 is a substituted amino group having the formula-N(R^{15})(CH₂)₉ R^{16} , R^6 is -H.

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In another embodiment of the sixth group of compounds, Z¹, Z³, Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted amino group having the formula -N(R¹⁵)(CH₂)_qR¹⁶ or the formula $-N(R^{15})C(H)(alkyl)((CH₂)_qR^{16})$ where q is an integer selected from 0, 1, 2, or 3, R^{16} is selected from a methyl group, substituted and unsubstituted alkoxy groups, 5 substituted and unsubstituted amino groups such as -N(H)(alkyl) groups, -N(alkyl)₂ groups and the like, substituted and unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and R¹⁵ is selected from -H; substituted and unsubstituted alkyl groups such as, but not limited to, methyl, ethyl, propyl, and isopropyl groups; -C(=O)-alkyl groups such as -C(=O)-CH₃ groups and the like; 10 -C(=O)-alkyl-N(H)(alkyl) groups such as -C(=O)-CH₂-N(H)(alkyl) groups and the like: -C(=O)-alkyl-N(alkyl)2 groups such as -C(=O)-CH2-N(alkyl)2 groups and the like; -C(=O)-alkyl- $N(R^{15a'})(R^{15b'})$ groups such as -C(=O)- CH_2 - $N(alkyl)_2$ groups and the like -C(=O)-alkyl-heterocyclyl groups such as -C(=O)-CH₂-heterocyclyl groups and the like such as -C(=O)-CH₂-(1-piperazinyl) groups and the like; 15 -C(=O)-heterocyclyl groups; -C(=O)-aryl groups; -C(=O)-alkyl-O-alkyl groups such as -C(=O)-CH₂-O-alkyl groups; -C(=O)-alkyl-S-alkyl groups such as -C(=O)-CH₂-S-alkyl groups and the like; and the like where R^{15a'} is selected from -H, and substituted and unsubstituted alkyl groups, and R^{15b'} is selected from -H, -SO₂-alkyl, -SO₂-aryl, -C(=O)-alkyl, -C(=O)-aryl, heterocyclyl groups such as 2-20 pyridyl groups and the like, heterocyclylalkyl groups, arylalkyl groups, alkyl groups, and -C(=O)-alkyl-halogen groups.

In another embodiment of the sixth group of compounds, Z¹, Z², Z⁴, R¹, R², R³, R⁵, and R⁸ have any of the values in previous embodiments, Z³ is C, and R⁷ is a substituted or unsubstituted heterocyclyl group. In some embodiments of the sixth group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is selected from substituted or unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyridyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted and piperidinyl groups, substituted and unsubstituted and unsubs

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unsubstituted imidazolyl groups, substituted and unsubstituted 1-aza-4oxacycloheptane groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted 1,4-diazacycloheptane groups, substituted and unsubstituted 2.5diazabicyclo[2.2.1]heptane groups, substituted and unsubstituted 1,4-5 diazabicyclo[2.2.2]octane groups, substituted or unsubstituted 1,4diazabicyclo[4.3.0]nonane group, and substituted or unsubstituted 1,4diazacycloheptane groups. In still other embodiments of the sixth group of compounds where R⁷ is a heterocyclyl group, the heterocyclyl group is an unsubstituted morpholine group; a dialkyl substituted morpholinyl group such as, 10 but not limited to, a dimethyl substituted morpholinyl group, and the like, such as, but not limited to, a 3,5-dimethyl substituted morpholinyl group; a hydroxy substituted morpholinyl group; a hydroxyalkyl substituted morpholinyl group; an aryl substituted morpholinyl group; an aminoalkyl substituted morpholinyl group including dialkylaminoalkyl substituted morpholinyl groups such as, but not limited 15 to, dimethylaminomethyl substituted morpholinyl groups and the like such as, but not limited to, a morpholinyl group that is substituted on a ring carbon bonded to the ring O atom with a dimethylaminomethyl group and is substituted with a methyl group on the carbon bonded to the ring N atom which carbon is not bonded to the carbon bearing the dimethylaminomethyl group and the like; a heterocyclyl 20 substituted morpholinyl group; an unsubstituted piperazine group; a dialkyl substituted piperazinyl group such as, but not limited to, a dimethyl substituted piperazinyl group, and the like such as a 3,5-dimethyl substituted piperazinyl group and the like; a monoalkyl substituted piperazinyl group such as a 3-alkyl substituted piperazinyl group, an N-alkyl substituted piperazinyl group, and the like such as, 25 but not limited to, a 3-methyl substituted piperazinyl group, a N-alkyl substituted piperazinyl group, such as, but not limited to, N-methyl, N-ethyl, N-isopropyl substituted piperazinyl groups and the like; a hydroxyalkyl substituted piperazinyl group such as, but not limited to, hydroxyethyl and hydroxymethyl substituted piperazinyl groups and the like such as, but not limited to, N-hydroxyethyl substituted piperazinyl groups and the like; an aryl substituted piperazinyl group; a 30

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heterocyclyl substituted piperazinyl group such as, but not limited to, 2-, 3-, and 4-(2-, 3-, and 4-piperidinyl) substituted piperazinyl groups and 2-, 3-, and 4-(2-, 3-, and 4-pyridyl) substituted piperazinyl groups and the like; a -CH₂C(=O)O-alkyl substituted piperazinyl group; a -C(=0)-alkyl substituted piperazinyl group such as, but not limited to, a -C(=O)-ethyl or a -C(=O)-methyl substituted piperazinyl 5 group, and the like such as a piperazinyl group where the -C(=O)-ethyl or the -C(=O)-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a -C(=0)O-alkyl substituted piperazinyl group such as, but not limited to, a -C(=0)-O-ethyl or a -C(=0)-O-methyl substituted piperazinyl group, and the like such as a piperazinyl group where the -C(=O)-O-10 ethyl or the -C(=0)-O-methyl substitution is on one of the piperazinyl N atoms and the other N atom is bonded to Z³, and the like; a cycloalkyl substituted piperazinyl group such as, but not limited to, a cyclohexyl and cyclopentyl substituted piperazinyl group and the like such as, but not limited to, a N-cyclohexyl substituted piperazinyl group and the like; an unsubstituted piperidine group; an alkyl 15 substituted piperidinyl group such as, but not limited to, 2-, 3-, and 4- alkyl substituted piperidinyl groups, and the like such as, but not limited to, 2-, 3-, and 4hydroxyalkyl substituted piperidinyl groups and the like such as, but not limited to, 2-, 3-, and 4-hydroxymethyl substituted piperidinyl groups and the like; a hydroxy 20 substituted piperidinyl group such as 2-, 3-, and 4-hydroxy substituted piperidinyl groups; a hydroxyalkyl substituted piperidinyl group; an aryl substituted piperidinyl group such as, but not limited to, a 4-aryl substituted piperidinyl group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both an aryl group and a hydroxy group and the like such as, but not limited to, a piperidinyl group that is substituted in the 4 position with both a hydroxy group 25 and a phenyl group; a cycloalkyl substituted piperidinyl group; a heterocyclyl substituted piperidinyl group such as, but not limited to, a piperidinyl substituted piperidinyl group and the like such as, but not limited to, 4-piperidinyl substituted piperidinyl groups, 4-(2(3H)-benzimidazolone) substituted piperidinyl group, and 30 the like; an unsubstituted pyrrolidinyl group; an alkyl substituted pyrrolidinyl group

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such as, but not limited to, a methyl substituted pyrrolidinyl group, a heterocyclylalkyl substituted pyrrolidinyl group, and the like such as, but not limited to, a 2-methyl substituted pyrrolidinyl group, a 2-pyrrolidinylmethyl substituted pyrrolidinyl group, and the like; an amino substituted pyrrolidinyl group such as. but not limited to, a dialkylamino substituted pyrrolidinyl group such as, but not limited to, 2- and 3-dialkylamino substituted pyrrolidinyl groups and the like such as, but not limited to, 2- and 3- substituted N,N-dimethylamino substituted pyrrolidinyl groups and the like such as, but not limited to, a pyrrolidinyl group that is substituted with both an alkyl group and an N,N-dimethylamino group and the 10 like such as, but not limited to, a pyrrolidinyl group that is substituted with a methyl group in the 2 position and with a N,N-dimethylamino group in the 4 position; a hydroxy substituted pyrrolidinyl group such as, but not limited to, 2- and 3-hydroxy substituted pyrrolidinyl groups; a heterocyclylalkyl substituted pyrrolidinyl group; substituted and unsubstituted pyrrolyl groups; substituted and unsubstituted 2,5diazabicyclo[2.2.1]heptane groups; an alkyl substituted 15 2.5-diazabicyclo[2.2.1]heptane group such as, but not limited to, a N-methyl substituted 2,5-diazabicyclo[2.2.1]heptane group and the like; a substituted or unsubstituted 1,4-diazabicyclo[4.3.0]nonane group; and a substituted or unsubstituted 1,4-diazacycloheptane group such as, but not limited to, an alkyl 20 substituted 1,4-diazacycloheptane group and the like, such as, but not limited to, an N-alkyl substituted 1,4-diazacycloheptane substituted group and the like such as, but not limited to, a N-methyl substituted 1,4-diazacycloheptane group and the like. In still other embodiments of the sixth group of compounds where R⁷ is a substituted or unsubstituted heterocyclyl group, R⁶ is -H.

In another embodiment of the sixth group of compounds, Z¹-Z⁴, R¹, R², and R³ have any of the values in previous embodiments, and one of R⁶ or R⁷ is a substituted or unsubstituted pyridyloxy group. In some such embodiments, one of R⁶ or R⁷ is substituted or unsubstituted 2-pyridyloxy group, a 3-pyridyloxy group, or a 4-pyridyloxy group. In other such embodiments, one of R⁶ or R⁷ is a (2-N-alkylamido-4-pyridyl)oxy group such as a (2-N-methylamido-4-pyridyl)oxy group or

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the like; or a (5-N-alkylamido-3-pyridyl)oxy group such as a (5-N-methylamido-3-pyridyl)oxy group, or the like.

Other more particular embodiments of the compounds of the invention having the general structure shown in I above are provided. Such compounds form a seventh group of compounds for which:

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C \equiv N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl 10 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=0)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted 15 -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, 20 substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-25 heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted

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heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

 R^2 is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino 10 groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups, substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted 15 -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and 20 unsubstituted -N(H)C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted 25 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted 30 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted

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(alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-5 heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl 10 groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-15 C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula -OCH₂Osuch that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms;

 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C=N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 20 -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 25 unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted 30

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-C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-alkylheterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 5 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl 10 groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and 15 unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

R⁴ is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl

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groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 5 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)heterocyclyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl 10 groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted heterocyclylalkylaminoalkyl groups, 15 substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

20 R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and

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unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted and unsubstituted aryloxy groups, substituted and unsubstituted and unsubstituted and unsubstituted dialkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and 15 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 20 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino 25 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

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'-C(=0)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N;

 R^8 is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R^8 is absent if Z^4 is N;

R⁹ is -H;

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R¹⁰ is selected from the group consisting of -H, and substituted and unsubstituted alkyl groups; and

at least one of Z² or Z³ is C and at least one of R⁶ or R⁷ is selected from the group consisting of substituted and unsubstituted piperidinyl substituted heterocyclyl groups, substituted and unsubstituted heterocyclyl substituted piperidinyl groups, substituted and unsubstituted hydroxymethyl substituted piperidinyl groups, dimethylaminoalkyl substituted pyrrolidinyl groups, substituted and unsubstituted 3-alkyl substituted piperazinyl groups, substituted and unsubstituted 3,5-dialkyl substituted piperazinyl groups, substituted and unsubstituted N-hydroxyalkyl substituted piperazinyl groups, substituted and unsubstituted 1,4-diazacycloheptyl groups, substituted and unsubstituted 1-aza-4oxacycloheptyl groups, substituted and unsubstituted N-ethylpiperazinyl groups, substituted and unsubstituted N-isopropylpiperazinyl groups, substituted and unsubstituted N-sec-butylpiperazinyl groups, substituted and unsubstituted N-2pyridyl substituted piperazinyl groups, substituted and unsubstituted N-3-pyridyl substituted piperazinyl groups, substituted and unsubstituted N-4-pyridyl substituted piperazinyl groups, substituted and unsubstituted N(H)-CH2-pyridyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted 3alkyl substituted morpholinyl groups, substituted and unsubstituted 3,5-dialkyl substituted morpholinyl groups, dialkylamino substituted pyrrolidinyl groups,

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pyrrolidinyl groups substituted with both dialkylamino and alkyl groups, substituted and unsubstituted 4-hydroxy substituted piperidinyl groups, substituted and unsubstituted 4-aryl substituted piperidinyl groups, substituted and unsubstituted 4hydroxy-4-phenyl substituted piperidinyl groups, substituted and unsubstituted cyclohexylpiperazinyl groups, substituted and unsubstituted cyclopentylpiperazinyl groups, substituted and unsubstituted N-alkyl substituted diazabicycloalkane groups. substituted and unsubstituted -N(CH3)(N-alkyl(4-piperidinyl)) groups, substituted and unsubstituted piperazinyl groups further substituted with a -C(=0)-alkyl group on one of the N atoms of the piperazinyl group, substituted and unsubstituted 10 -N(H)CH2CH2-imidazolyl groups, substituted and unsubstituted -N(H)CH2CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2CH2-morpholinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH2CH2-pyridyl groups, substituted and unsubstituted -N(H)CH2CH2-15 imidazolyl groups, substituted and unsubstituted -N(H)CH2CH2-pyrrolidinyl groups, substituted and unsubstituted -N(H)CH2CH2-morpholinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted -N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted -N(H)CH2CH2pyridyl groups, substituted and unsubstituted cyclobutylpiperazinyl groups, 20 substituted and unsubstituted -OCH2-pyrrolidinyl groups, substituted and unsubstituted -OCH2CH2-pyrrolidinyl groups, substituted and unsubstituted -OCH2CH2CH2-pyrrolidinyl groups, substituted and unsubstituted piperazinyl groups further substituted with a -CH₂C(=0)-O-alkyl group bonded to one of the N atoms of the piperazinyl group, substituted and unsubstituted piperazinyl groups further 25 substituted with a -C(=O)-O-alkyl group bonded to one of the N atoms of the piperazinyl group, substituted and unsubstituted hydroxypyrrolidinyl groups, substituted and unsubstituted hydroxypiperidinyl groups, substituted and unsubstituted -OCH2-pyridyl groups, substituted and unsubstituted piperidinylamino

groups, substituted and unsubstituted pyridyloxy groups with a -C(=O)-N(H)(alkyl)

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group bonded to a carbon atom of the pyridine ring of the pyridyloxy group, and substituted and unsubstituted pyridyloxy groups with a $-C(=O)-N(alkyl)_2$ group bonded to a carbon atom of the pyridine ring of the pyridyloxy group.

In some embodiments, R¹⁰ is -H. In other embodiments, R¹⁰ is an unsubstituted alkyl group having from 1 to 6 carbon atoms such as a methyl, ethyl, propyl, i-propyl group, or the like. In some such embodiments, R¹⁰ is a -CH₃ group.

In one embodiment of the seventh group of compounds, each of Z^1 , Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the seventh group of compounds, Z^1 is N and each of Z^2 , Z^3 , and Z^4 are C.

In another embodiment of the seventh group of compounds, Z^1 and Z^3 are both N and Z^2 and Z^4 are both C.

In another embodiment of the seventh group of compounds, Z^3 is N and each of Z^1 , Z^2 , and Z^4 are C.

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In another embodiment of the seventh group of compounds, Z^1 - Z^4 have any of the values in previous embodiments, and R^1 is selected from -H, -F, -Cl, and -Br.

In another embodiment of the seventh group of compounds, Z¹-Z⁴

20 have any of the values in previous embodiments, and R¹ is a substituted and unsubstituted heterocyclylamino group. In some such embodiments, R¹ is a substituted and unsubstituted heterocyclylamino groups. In some embodiments, R¹ is a substituted and unsubstituted heterocyclylamino group such as, but not limited to, substituted and unsubstituted pyrroldinylalkylamino groups and the like, such as, but not limited to, substituted and unsubstituted pyrroldinylmethylamino groups and the like.

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In another embodiment of the seventh group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is selected from -H, -F. -Cl. -CO2H, substituted and unsubstituted alkyl groups, substituted and unsubstituted -C(=0)O-alkyl groups, substituted and unsubstituted -C(=0)N(H)alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted 5 and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=0)-heterocyclyl groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted -10 N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R² and R3 are a group of formula -OCH2O- such that R2 and R3 define a fused 5-15 membered ring that includes 2 oxygen atoms.

In another embodiment of the seventh group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is -H.

In another embodiment of the seventh group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is an unsubstituted alkoxy group having from 1 to 4 carbon atoms.

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In another embodiment of the seventh group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a -OMe, -OEt, -O-i-Pr, or -OCH₂CH(CH₃)₂ group.

25 In another embodiment of the seventh group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted arylalkoxy, a substituted or unsubstituted aryloxy group, or a substituted or unsubstituted heterocyclyoxy group.

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In another embodiment of the seventh group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted benzyloxy group, a substituted or unsubstituted phenoxy group, or a substituted or unsubstituted pyridyloxy group.

In another embodiment of the seventh group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is an unsubstituted alkyl group having from 1 to 4 carbon atoms.

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In another embodiment of the seventh group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a methyl group.

In another embodiment of the seventh group of compounds, Z^1-Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted -N(H)C(=O)-N(H)-alkyl-aryl group.

In another embodiment of the seventh group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of substituted and unsubstituted alkylamino groups, dialkylamino groups, cycloalkylamino groups, heterocyclylamino groups, heterocyclylalkylamino groups, arylalkylamino groups, arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups. In some embodiments, the substituted and unsubstituted alkylamino groups are substituted and unsubstituted aminoalkylamino groups such as, but not limited to, dialkylaminoalkylamino and the like. In some such embodiments the substituted and unsubstituted heterocyclylalkylamino groups are substituted and unsubstituted heteroarylalkylamino groups. In some embodiments, the heterocyclylalkylamino groups include, but are not limited to, substituted and unsubstituted pyrrolidinylalkylamino groups such as, but not limited to, substituted and unsubstituted pyrrolidinylmethylalkylamino groups and the like; substituted and unsubstituted thiazolylalkylamino groups such as, but not limited to substituted and unsubstituted thiazolylmethylamino groups and the like; substituted and

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unsubstituted imidazolylalkylamino groups such as, but not limited to, imidazolylmethylamino groups and the like; substituted and unsubstituted furanylalkylamino groups such as, but not limited to, substituted and unsubstituted furanylmethylamino groups, and the like; and the like. In other such embodiments, the heterocyclylamino groups are substituted and unsubstituted heteroarylamino groups. In other such embodiments, the substituted and unsubstituted heterocyclylamino groups are substituted and unsubstituted arylalkylheterocyclylamino groups.

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In another embodiment of the seventh group of compounds, Z¹-Z⁴

and R¹ have any of the values in previous embodiments, and R² is a substituted or unsubstituted amino group selected from the group consisting of isopropylamino groups, 3-(N,N-dimethylamino)propylamino groups, pyrrolidinylmethylamino groups, arylmethylamino groups, arylalkoxyarylmethylamino groups, aryloxyarylmethylamino groups, and pyridylmethylamino groups, and pyridylamino groups.

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In another embodiment of the seventh group of compounds, Z^1 - Z^4 and R^1 have any of the values in previous embodiments, and R^2 is a substituted or unsubstituted heterocyclyl groups. In some such embodiments R^2 is a substituted or unsubstituted benzimidazolyl group or is a substituted or unsubstituted pyrazolyl group.

In another embodiment of the seventh group of compounds, Z¹-Z⁴ and R¹ have any of the values in previous embodiments, and R² and R³ are a group of formula -OCH2O- such that R² and R³ define a fused 5-membered ring that includes 2 oxygen atoms.

In another embodiment of the seventh group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is selected from -H, -F, -Cl, and -OMe.

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In another embodiment of the seventh group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -H.

In another embodiment of the seventh group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of -F, -C1, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-alkyl groups, substituted and unsubstituted -N(H)C(\equiv O)N(H)-aryl groups and substituted and unsubstituted -C(\equiv O)N(H)-alkyl-heterocyclyl groups; or R^2 and R^3 are a group of formula -OCH₂O- such that R^2 and R^3 define a fused 5-membered ring that includes 2 oxygen atoms.

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In another embodiment of the seventh group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is selected from the group consisting of substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted -N(H)C(=O)N(H)-aryl groups. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)CH₂CH₃ group, a substituted or unsubstituted -N(H)C(=O)N(H)CH(CH₃)₂ group, a substituted or unsubstituted -N(H)C(=O)N(H)C(CH₃)₃ group, or a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group or the like. In some such embodiments, R^3 is a substituted or unsubstituted -N(H)C(=O)N(H)-aryl group such as, but not limited to, a -N(H)C(=O)N(H)-(2-methoxyphenyl) group, a-N(H)C(=O)N(H)-(trifluoromethylphenyl) group, or the like.

In another embodiment of the seventh group of compounds, Z¹-Z⁴, R¹, and R² have any of the values in previous embodiments, and R³ is a substituted amino group selected from substituted or unsubstituted arylalkylamino groups such as, but not limited to, phenylalkylamino groups, (halo)(alkoxy)arylalkylamino groups, such as, but not limited to 2-fluoro-5-methoxyphenylmethylamino groups, monoalkoxyarylalkylamino groups, dialkoxyarylalkylamino groups, and the like, such as, but not limited to, 2,5-dialkoxyarylalkylamino groups and the like such as,

but not limited to 2,5-dialkoxyarylmethylamino groups, substituted and unsubstituted arylalkoxyarylalkylamino groups such as, but not limited to substituted and unsubstituted arylalkoxyarylmethylamino groups and the like, such as, but not limited to, substituted and unsubstituted arylmethoxyarylmethylamino groups and the like, such as, but not limited to substituted and unsubstituted 5 fluoroarylmethoxyarylmethylamino groups and the like, such as, but not limited to, substituted and unsubstituted 4-fluorophenylmethoxyphenyl-methylamino groups and the like; substituted and unsubstituted heterocyclylalkylamino groups including heteroarylalkylamino groups such as, but not limited to substituted and unsubstituted 10 thiazolylalkylamino groups, benzimidazolylalkylamino groups such as, but not limited to N-methylbenzimidazolylalkylamino groups and the like, imidazolylalkylamino groups such as, but not limited to phenylimidazolylalkylamino groups, ethylmethylimidazolylalkylamino groups, and the like, substituted and unsubstituted quinolinylalkylamino groups, such as, but not limited to substituted and unsubstituted quinolinylmethylamino groups and the like, such as, but not 15 limited to alkoxyquinolinylmethylamino groups and the like, such as, but not limited to substituted and unsubstituted 4-alkoxy-2-quinolinylmethylamino groups and the like, and furanylalkylamino groups, and the like.

In another embodiment of the seventh group of compounds, Z^1-Z^4 , 20 R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -F.

In another embodiment of the seventh group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -Cl.

In another embodiment of the seventh group of compounds, Z^1-Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is -OMe.

In another embodiment of the seventh group of compounds, Z^1 - Z^4 , R^1 , and R^2 have any of the values in previous embodiments, and R^3 is a substituted and unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups where the heterocyclyl

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group of the -C(=O)N(H)-alkyl-heterocyclyl groups is selected from the group consisting of morpholinyl, piperazinyl, and piperidinyl groups.

In another embodiment of the seventh group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is H. In some such embodiments, R^8 is also H.

In another embodiment of the seventh group of compounds, Z^2 - Z^4 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^1 is C, and R^5 is -CH₃.

In another embodiment of the seventh group of compounds, Z²-Z⁴,

R¹, R², and R³ have any of the values in previous embodiments, Z¹ is C, and R⁵ is morpholine.

In another embodiment of the seventh group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is H.

In another embodiment of the seventh group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is -CH₃.

In another embodiment of the seventh group of compounds, Z^1 - Z^3 , R^1 , R^2 , and R^3 have any of the values in previous embodiments, Z^4 is C, and R^8 is morpholine.

In another embodiment of the seventh group of compounds, at least one of R⁶ or R⁷ is selected from the group consisting of piperidinyl substituted piperidinyl groups such as 4-piperidinylpiperidinyl groups or the like, 4-hydroxymethylpiperidinyl groups, 3-dimethylaminomethylpyrrolidinyl groups, 3-alkyl substituted piperazinyl groups, N-hydroxymethylpiperazinyl groups, N-hydroxymethylpiperazinyl groups, N-hydroxymethylpiperazinyl groups, N-hydroxypropylpiperazinyl groups, N-methyl substituted 1,4-diazacycloheptyl

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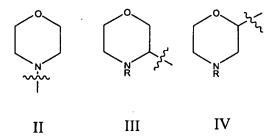
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groups, N-ethylpiperazinyl groups, N-isopropylpiperazinyl groups, N-secbutylpiperazinyl groups, unsubstituted piperazinyl groups, N-(2-pyridyl)piperazinyl groups, N-(3-pyridyl)piperazinyl groups, N-(4-pyridyl)piperazinyl groups, N(H)-CH₂-pyridyl groups, imidazolyl groups, unsubstituted morpholinyl groups, 3alkylmorpholinyl groups, 3,5-dialkylmorpholinyl groups, 2-dimethylaminopyrrolidinyl groups, 2-methyl-4-dialkylaminopyrroldinyl groups, 4-hydroxypiperidinyl groups, 4-arylpiperidinyl groups, 4-hydroxy-4-phenylpiperidinyl groups, cyclohexylpiperazinyl groups, cyclopentylpiperazinyl groups, N-methyl substituted diazabicycloalkane groups, -N(CH₃)(N-alkyl(4-piperidinyl)) groups, piperazinyl groups further substituted with 10 a -C(=0)-methyl group on one of the N atoms of the piperazinyl group, -N(H)CH2CH2CH2-imidazolyl groups, -N(H)CH2CH2CH2-pyrrolidinyl groups, -N(H)CH2CH2CH2-morpholinvl groups, -N(H)CH2CH2CH2-piperazinvl groups, -N(H)CH2CH2-piperidinyl groups, and -N(H)CH2CH2-pyridyl groups. In some such embodiments, at least one of R⁶ or R⁷ is selected from the group 15 consisting of 4-piperidinylpiperidinyl groups, 4-hydroxymethylpiperidinyl groups, 3-dimethylaminomethylpyrrolidinyl groups, 3,5-dimethyl substituted piperazinyl groups, N-methyl substituted 1,4-diazacycloheptyl groups, N-(2-pyridyl)piperazinyl groups, N(H)-CH2-(4-pyridyl) groups, imidazolyl groups, unsubstituted morpholinyl groups, 3-methylmorpholinyl groups, 3,5-dimethylmorpholinyl groups, 20 2-dimethylaminopyrrolidinyl groups, 2-methyl-4-dimethylaminopyrroldinyl groups, 4-hydroxy-4-phenylpiperidinyl groups, cyclohexylpiperazinyl groups, N-methyl substituted diazabicycloalkane groups, -N(CH3)(N-methyl(4-piperidinyl)) groups, piperazinyl groups further substituted with a -C(=O)-methyl group on one of the N 25 atoms of the piperazinyl group, -N(H)CH2CH2CH2-imidazolyl groups, -N(H)CH2CH2CH2-pyrrolidinyl groups, -N(H)CH2CH2-morpholinyl groups, -N(H)CH2CH2CH2-piperazinyl groups, -N(H)CH2CH2-piperidinyl groups, and

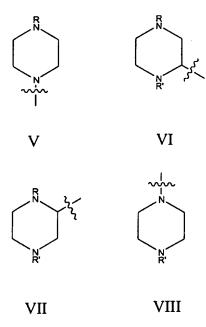
-N(H)CH2CH2CH2-pyridyl groups.

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The heterocyclic groups of the present invention may be attached in various ways. For example, where R^6 is a heterocyclyl group such as morpholine, the morpholine may be attached to Z^2 as shown below in Structures II, III, and IV.



As a further example, where R^6 is a piperazine group, the piperazine may be attached to Z^2 as shown below in Structures V, VI, VII, and VIII.



As a further example, where R^6 is a pyrrolidinyl group, then the pyrrolidinyl group may be attached to Z^2 as shown below in structures IX, X, and XI.

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The indazole benzimidazoles of the present invention may generally be assembled by coupling a suitably substituted indazole fragment with a suitably substituted 2-amino aniline or 2-nitro aniline compound. In one method, shown in Scheme 1, an indazole-3-carboxylic acid is reacted with POCl₃ to form a dimer. The resulting dione is then heated in the presence of a suitably substituted diamine to form the desired indazole benzimidazole adduct. If a nitro aniline is used in place of the diamine, an additional reduction and cyclodehydration step is required to effect the ring closure. Alternatively a diamine having one protected amine group may be reacted in place of the diamine. Formation of the indazole benzimidazole by this procedure will include a deprotection and cyclodehydration to afford the desired indazole benzimidazole compound. These reactions may be conducted in aromatic solvents such as toluene and non-nucleophilic bases such as trialkylamines such as triethylamine may be employed.

Scheme 1

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Therefore, according to one embodiment, the invention provides a method for synthesizing a substituted or unsubstituted indazole benzimidazole. The method includes: (a) reacting a dimer formed from two molecules of an indazole-3-carboxylic acid, wherein the six membered benzene ring of the indazole-3-carboxylic acid may be substituted or unsubstituted, with an amino compound selected from the group consisting of:

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- (i) a diaminobenzene derivative comprising a benzene ring and at least two amine groups bonded to adjacent carbon atoms in the benzene ring, wherein the benzene ring may be further substituted or may comprise 1,2-diaminobenzene, and further wherein the substituted or unsubstituted indazole benzimidazole is formed by reaction with the dimer;
- (ii) a nitroaminobenzene derivative comprising a benzene ring, at least one nitro group, and at least one amine group, wherein the at least one amine group is bonded to a carbon atom in the benzene ring that is adjacent to another carbon atom in the benzene ring to which the at least one nitro group is bonded, further wherein the benzene ring may be further substituted or may comprise 1-amino-2-nitrobenzene, and further wherein an amide comprising a nitro group is formed by reaction with the dimer;
- (iii) a first (protected amino)(amino)benzene derivative comprising a benzene ring, at least one protected amine group, and at least one -NH2 group, wherein the at least one protected amine group is bonded to a first carbon atom in the benzene ring that is adjacent to a second carbon atom in the benzene ring to which the at least one -NH2 group is bonded, further wherein the benzene ring may be further substituted or may only include H atoms bonded to the four other carbon atoms of the benzene ring, and further wherein an amide comprising at least one protected amine group is formed by reaction with the dimer; and
 - (iv) a second (protected amino)(amino)benzene derivative comprising a benzene ring, at least one protected amine group, and at least one

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-NH₂ group, wherein the at least one protected amine group is bonded to a first carbon atom in the benzene ring that is adjacent to a second carbon atom in the benzene ring to which the at least one -NH₂ group is bonded, further wherein the benzene ring may be further substituted or may only include H atoms bonded to the four other carbon atoms of the benzene ring, further wherein the protected amine group comprises a protecting group that is removed during the reaction with the dimer such that the substituted or unsubstituted indazole benzimidazole is formed by the reaction with the dimer,

wherein, if the dimer is reacted with the nitroaminobenzene derivative, the method further comprises (b):

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(b) reducing the nitro group of the amide comprising the nitro group and cyclodehydrating to form the substituted or unsubstituted indazole benzimidazole;

and further wherein, if the dimer is reacted with the first (protected amino)(amino)benzene derivative, then the method further comprises (c):

(c) removing the protecting group from the amide comprising the at least one protected amine group and cyclodehydrating to form the substituted or unsubstituted benzimidazole.

In some embodiments, the dimer is reacted with the diaminobenzene derivative, the nitroaminobenzene derivative, the first (protected amino)(amino)benzene derivative, or the second (protected amino)(amino)benzene derivative in a toluene solution which may be a refluxing toluene solution in some embodiments. In some embodiments, the the dimer is reacted with the diaminobenzene derivative, the nitroaminobenzene derivative, the first (protected amino)(amino)benzene derivative at a temperature of greater than 85°C whereas in other embodiments, the temperature ranges from about 95°C to about 111°C, from about 95°C to about 100°C.

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In some embodiments, the method includes reacting the dimer with a salt such as hydrochloride, hydrobromide, dihydrochloride, dihydrobromide, or the like salt of the diaminobenzene derivative, the nitroaminobenzene derivative, the first (protected amino)(amino)benzene derivative, or the second (protected amino)(amino)benzene derivative. In other embodiments, the diaminobenzene derivative, the nitroaminobenzene derivative, the first (protected amino)(amino)benzene derivative, or the second (protected amino)(amino)benzene derivative is reacted with the dimer in the presence of a base such as, but not limited to, triethylamine, tripropylamine, tributylamine, ethyldipropylamine,

In some embodiments, the method includes reacting the indazole-3-carboxylic acid with a reagent affecting the conversion of the acid to an acid halide or anhydride such as, but not limited to, cyanuric fluoride, tetramethylfluoroformamidinium hexafluorophosphate, cyanuric chloride, SOCl₂, PCl₃, PCl₅, PBr₃, PBr₅, POCl₃, carbonyl diimidazole/HCl, Oxalyl chloride, and carbodiimides, followed by in situ dimerization.

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In some embodiments in which the nitroaminobenzene derivative is reacted with the dimer, the method includes reducing the nitro group of the amide with hydrogen using a hydrogenation catalyst such as, but not limited to, Pd on carbon, Pt on carbon, or the like. In some such embodiments, the catalyst is Pd on carbon. In some such embodiments, the reduced product is cyclodehydrated by treating the reduced product with an acid such as, but not limited to, acetic acid. In some cases the reduced product is cyclodehydrated by treating the reduced product with sodium acetate and acetic acid and heating such as at a reflux temperature. In some embodiments in which the first (protected amino)(amino)benzene derivative is reacted with the dimer, cyclodehydrating includes reacting the amine formed by removal of the protecting group with an acid such as, but not limited to, acetic acid. In some cases the amine formed by removal of the protecting group is cyclodehydrated by treating the reduced product with sodium acetate and acetic acid

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and heating such as at a reflux temperature. In some cases, the amide comprising the protected amine group formed by reaction of the first (protected amino)(amino)benzene derivative with the dimer is removed and the product is cyclodehydrated, in one procedure, using an acid. Most commonly used protective groups for amines are stable to the reaction with the dimer. Boc may come off during the reaction with the dimer, but only if the temperature is maintained at from 130-150°C or higher. Examples of protective groups for the amines that are stable upon reaction with the dimer include, but are not limited to, carbamates such as, but not limited to, methyl ethyl, t-butyl, benzyl, and 9-fluorenylmethyl carbamates and the like; amides such as, but not limited to, acetamide, chloroacetamide, trifluoroacetamide, benzamide and the like; sulfonamides such as, but not limited to, benzenesulfonamide, p-toluenesulfonamide, trifluoromethanesulfonamide, and the like; and groups such as, but not limited to, N-allyl, N-benzyl, N-o-nitrobenzyl, Np-methoxybenzyl, N-2,4-dimethoxybenzyl, N-triphenylmethyl, SEM, and the like. Groups which are sensitive to acids such as, but not limited to, N-2,4dimethoxybenzyl, N-triphenylmethyl, may come off during cyclodehydration when it is performed in refluxing AcOH. If the cyclodehydration is performed in the presence of a non nucleophilic base such as triethylamine, some carbamates such as, but not limited to, 9-fluorenylmethyl carbamate and 2,4-dichlorobenzyl carbamate may be cleaved.

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In some embodiments, the indazole-3-carboxylic acid used to form the dimer has the formula XII where R¹, R², R³, R⁴, and R⁹ have any of the values set forth above with respect to the first, second, third, fourth, fifth, sixth, and seventh group of compounds having the formula I. Compound XII has the following structure.

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$$R^2$$
 R^3
 R^4
 R^9
XII

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In some embodiments, the dimer is a compound having the formula XIII where R¹, R², R³, and R⁴ have any of the values set forth above with respect to the first, second, third, fourth, fifth, sixth, and seventh group of compounds having the formula I. With respect to the indazole-3-carboxylic acid of formula XII and the dimer of formula XIII, one skilled in the art will recognize that certain nucleophilic R¹ through R⁴ groups may need to be protected with suitable protecting groups prior to formation of the dimer or prior to reaction with the the diaminobenzene derivative, the nitroaminobenzene derivative, the first (protected amino)(amino)benzene derivative, or the second (protected amino)(amino)benzene derivative. Compound of formula XIII have the following structure.

In some embodiments in which the diaminobenzene derivative is reacted with the dimer, the diaminobenzene derivative is a compound having the formula XIV where R⁵, R⁶, R⁷, and R⁸ have any of the values set forth above with respect to the first, second, third, fourth, fifth, sixth, and seventh group of compounds having the formula I. One skilled in the art will recognize that certain nucleophilic R⁵ through R⁸ groups may need to be protected with suitable protecting

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groups for reaction with the dimer. Compounds of formula XIV has the following structure.

$$R^5$$
 R^6
 R^7
 R^8
 XIV

In some embodiments in which the nitroaminobenzene derivative is
reacted with the dimer, the diaminobenzene derivative is a compound having the
formula XVA or XVB where R⁵, R⁶, R⁷, and R⁸ have any of the values set forth
above with respect to the first, second, third, fourth, fifth, sixth, and seventh group
of compounds having the formula I. One skilled in the art will recognize that
certain nucleophilic R⁵ through R⁸ groups may need to be protected with suitable
protecting groups for reaction with the dimer. Compounds of formula XVA and
XVB have the following structures.

$$R^{5}$$
 R^{6}
 R^{7}
 R^{8}
 R^{8}
 R^{7}

The indazole fragment may also be constructed from suitably substituted indoles *via* a nitrosation reaction to form a suitably substituted indazole-3-carbaldehyde as the key coupling precursor (Scheme 2). This strategy affords considerable flexibility in the synthesis of functionalized indazole benzimidazoles. By using appropriately substituted indole,1,2-diaminobenzene, or 1,2-diaminoheteroaryl starting materials, many of which are commercially available or

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may be easily made by one of skill in the art, a wide variety of desired indazole benzimidazole compounds may be synthesized. Without being bound to hypothesis, it is believed that a hemiaminal intermediate compound is initially obtained which is then cyclooxidized to provide the substituted and unsubstituted indazole benzimidazole compounds of the invention. The suitably substituted indazole-3carbaldehyde may alternatively be reacted with a suitably substituted monoprotected substituted or unsubstituted 1,2-diaminobenzene to form an imine that includes the protecting group. The intermediate imine product may then be deprotected and oxidatively cyclized to produce the desired indazole benzimidazole product. The suitably substituted indazole-3-carbaldehyde may also be reacted with a suitably substituted benzene bearing at least two amine groups one of which is protected with a suitable protecting group that provides a protected benzimidazole indazole product. Removal of the protecting group in such embodiments affords the indazole benzimidazole product. In another embodiment, the indazole-3-carbaldehyde may be reacted with a monoprotected substituted or unsubstituted 1,2-diaminobenzene derivative in a reaction in which the protecting group is lost and the indazole benzimidazole is formed. Generally, the O₂ for the oxidative cyclization step comes from that dissolved in the solvent in the reaction vessel. In one alternative embodiment, O2 may be bubbled through the reaction mixture. In other embodiments, compounds which provide a source for O₂ such as nitrobenzene may be used in the oxidative cyclization to form the indazole benzimidazole product.

Scheme 2

NaNO₂ / HCI

NaNO₂ / HCI

N O₂, toluene, EtOH,
$$\Delta$$

R

N
R

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In one embodiment, the invention provides a first alternative method for synthesizing a substituted or unsubstituted indazole benzimidazole. The method includes reacting a substituted or unsubstituted indazole-3-carbaldehyde with an amino compound selected from the group consisting of:

- 5 (i) a diaminobenzene derivative comprising a benzene ring and at least two amine groups bonded to adjacent carbon atoms in the benzene ring, wherein the benzene ring may be further substituted or may comprise 1,2-diaminobenzene, and further wherein the substituted or unsubstituted indazole benzimidazole is formed by reaction with the substituted or unsubstituted indazole-3-carbaldehyde;
 - (ii) a first (protected amino)(amino)benzene derivative comprising a benzene ring, at least one protected amine group, and at least one -NH2 group, wherein the at least one protected amine group is bonded to a first carbon atom in the benzene ring that is adjacent to a second carbon atom in the benzene ring to which the at least one -NH2 group is bonded, further wherein the benzene ring may be further substituted or may only include H atoms bonded to the four other carbon atoms of the benzene ring, and further wherein a N-protected substituted or unsubstituted indazole benzimidazole is formed by reaction with the substituted or unsubstituted indazole-3-carbaldehyde;

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20 (iii) a second (protected amino)(amino)benzene derivative comprising a benzene ring, at least one protected amine group, and at least one -NH2 group, wherein the at least one protected amine group is bonded to a first carbon atom in the benzene ring that is adjacent to a second carbon atom in the benzene ring to which the at least one -NH2 group is bonded, further wherein the benzene ring may be further substituted or may only include H atoms bonded to the four other carbon atoms of the benzene ring, and further wherein an imine comprising at least one protected amine group is formed by reaction with the substituted or unsubstituted indazole-3-carbaldehyde; and

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(iv) a third (protected amino)(amino)benzene derivative comprising a benzene ring, at least one protected amine group, and at least one -NH2 group, wherein the at least one protected amine group is bonded to a first carbon atom in the benzene ring that is adjacent to a second carbon atom in the benzene ring to which the at least one -NH2 group is bonded, further wherein the benzene ring may be further substituted or may only include H atoms bonded to the four other carbon atoms of the benzene ring, further wherein the protected amine group comprises a protecting group that is removed during the reaction with the substituted or unsubstituted indazole-3-carbaldehyde such that the substituted or unsubstituted indazole benzimidazole is formed by the reaction with the substituted or unsubstituted indazole-3-carbaldehyde,

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wherein, if the substituted or unsubstituted indazole-3-carbaldehyde is reacted with the first (protected amino)(amino)benzene derivative, the method further comprises (b):

(b) removing the protecting group from the N-protected substituted or unsubstituted indazole benzimidazole to form the substituted or unsubstituted indazole benzimidazole;

and further wherein, if the substituted or unsubstituted indazole-3-carbaldehyde is reacted with the second (protected amino)(amino)benzene derivative, then the method further comprises (c):

(c) removing the protecting group from the imine comprising the at least one protected amine group and oxidatively cyclizing to form the substituted or unsubstituted benzimidazole.

In other embodiments, the diaminobenzene derivative, the first

(protected amino)(amino)benzene derivative, the second (protected amino)(amino)benzene derivative, or the third (protected amino)(amino)benzene derivative is reacted with the indazole-3-carbaldehyde in the presence of a base such

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as, but not limited to, triethylamine, tripropylamine, tributylamine, ethyldipropylamine, propyldiethylamine, or the like.

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In some embodiments of the first alternative methods, the method includes reacting the indazole-3-carbaldehyde with the diaminobenzene derivative, the first (protected amino)(amino)benzene derivative, the second (protected amino)(amino)benzene derivative, or the third (protected amino)(amino)benzene derivative in an aromatic solvent such as toluene, an alcohol solvent such as ethanol, or a combination of these such as a 3:1 toluene ethanol mixture. In other embodiments, the diaminobenzene derivative, the first (protected amino)(amino)benzene derivative, or the third (protected amino)(amino)benzene derivative is reacted with the indazole-3-carbaldehyde at a temperature of greater than 85°C whereas in other embodiments, the temperature ranges from about 95°C to about 111°C, from about 95°C to about 105°C, or from about 98°C to about 110°C.

In some embodiments in which the first (protected amino)(amino)benzene derivative is reacted with the indazole-3-carbaldehyde to produce the N-protected indazole benzimidazole, the protected amino group is protected with a protecting group such as Bn, SEM, and the like. In some embodiments in which the second (protected amino)(amino)benzene derivative is reacted with the indazole-3-carbaldehyde to produce the imine, the protected amino group is protected with a protecting group such as Fmoc, Boc, and the like. In some embodiments in which the third (protected amino)(amino)benzene derivative is reacted with the indazole-3-carbaldehyde to produce the indazole benzimidazole, the protected amino group is protected with a protecting group such as TMS, TES, and the like.

In some embodiments, the indazole-3-carbaldehyde used to form the indazole benzimidazole is a compound having the formula XVI where R¹, R², R³, and R⁴ have any of the values set forth above with respect to the first, second, third,

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fourth, fifth, sixth, and seventh group of compounds having the formula I. Compound XVI has the following structure.

$$R^2$$
 R^3
 R^4
 R^4
 R^4
 R^4
 R^4
 R^4
 R^4

In some embodiments in which the diaminobenzene derivative is reacted with the indazole-3-carbaldehyde, the diaminobenzene derivative is a 5 compound having the formula XIV as set forth above where R⁵, R⁶, R⁷, and R⁸ have any of the values set forth above with respect to the first, second, third, fourth, fifth, sixth, and seventh group of compounds having the formula I. One skilled in the art will recognize that certain nucleophilic R⁵ through R⁸ groups may need to be 10 protected with suitable protecting groups for reaction with the indazole-3carbaldehyde. In addition, certain R¹-R⁴ groups such as -OH may require protection during reaction of the substituted indole with NaNO2/HCl and during reaction with the diamine in toluene. Groups such as -OH may be protected with a suitable protecting groups such as Cbz which may then be removed after the indazole-3-carbaldehyde has been reacted with the diamine. Such transformation 15 are well within the realm of those skilled in the art.

In some embodiments of the first alternative method of forming a substituted or unsubstituted indazole benzimidazole, the indazole-3-carbaldehyde, such as compounds of formula XVI, are formed by reacting a suitably substituted indole with NaNO2. In such procedures, the reaction is generally conducted in the dark. The reaction may be protected from light by, for example, covering the reaction vessel with an opaque material such as aluminum foil or the like. In such procedures, a substituted or unsubstituted indole is generally added to a reaction vessel that includes an aqueous solution of NaNO2 at an acidic pH such as at a pH

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ranging from at or about 2 to a pH of at or about 3. In one embodiment, the pH is at or about 2.5. The NaNO2 solution is generally made acidic by adding an acid such as HCl or HBr although other acids may be employed for this purpose. An organic solvent such as dioxane or tetrahydrofuran may be added to the aqueous NaNO2 solution along with the indole or prior to adding the indole. Generally, the indole is added slowly to the reaction vessel that contains the NaNO2 solution. Suitable indoles for use in the synthesis of the indazole-3-carbaldehydes typically are compounds having the formula XVII where R¹ through R⁴ have any of the values set forth above with respect to the first, second, third, fourth, fifth, sixth, and seventh groups of compound of formula I. Compounds of formula XVII have the following structure.

$$\mathbb{R}^2$$
 \mathbb{R}^3
 \mathbb{R}^4
 \mathbb{R}^4

XVII

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A wide variety of indoles are commercially available for use in preparing the indazole-3-carbaldehydes of formula XVI. Examples of R¹ groups in commercially available indoles include, but are not limited to, -H, -F, -Cl, -CH₃, -CF₃, -OMe, -CO₂Me, -CO₂Et, -OBn, -C≡N, and the like. Examples of R² groups of commercially available indoles include, but are not limited to, -H, -F, -Cl, -Br, -OMe, -CF₃, and the like. Examples of R³ groups of commercially available indoles include, but are not limited to, -H, -F, -Cl, -OMe, -OBn, -CF₃, -C≡N, and the like. Examples of R⁴ groups of commercially available indoles include, but are not limited to, -H, -F, -Cl, -Br, -Et, -OMe, -CO₂Me, -CO₂Et, -OBn, -NO₂, and the like.

Scheme 3 illustrates just a few of the methods that may be used to produce a variety of 1,2-diamino benzenes. Halo (X = halogen) nitroanilines may be reacted with a wide variety of nucleophiles (Nu') such as alcohols and amines to produce functionalized nitroanilines which may subsequently be reduced to diamines. The alcohol moiety of a nitroamino phenol may be modified using known methods to introduce a broad range of substituents into a diamine for subsequent inclusion in an indazole benzimidazole compound.

Scheme 3

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In addition to the above schemes, it should be noted that various groups, including, but not limited to, hydroxyl groups and amine groups may be

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introduced into the indazole benzimidazole compounds of the present invention as protected groups using traditional protecting group chemistry. The use of standard protecting groups and the removal of such groups is well known in the art and various such groups may be used to prepare compounds in accordance with the present invention.

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The instant invention also provides for compositions which may be prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers thereof, with pharmaceutically acceptable carriers, excipients, binders, diluents or the like to treat or ameliorate a variety of disorders related to the activity of VEGF-RTK, more particularly angiogenesis associated with cancer or related to the activity of KDR, Flt-1, Flk-1, bFGFR, GSK-3, NEK-2, CHK-1, cdc 2, Tie-2, and PDGF. The compositoins of the inventions may be used to create formulations and to inhibit tyrosine kinases and serine/threonine kinases. Such compositions can be in the form of, for example, granules, powders, tablets, capsules, syrup, suppositories, injections, emulsions, elixirs, suspensions or solutions. The instant compositions can be formulated for various routes of administration, for example, by oral administration, by nasal administration, by rectal administration, subcutaneous injection, intravenous injection, intramuscular injections, or intraperitoneal injection. The following dosage forms are given by way of example and should not be construed as limiting the instant invention.

For oral, buccal, and sublingual administration, powders, suspensions, granules, tablets, pills, capsules, gelcaps, and caplets are acceptable as solid dosage forms. These can be prepared, for example, by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers thereof, with at least one additive such as a starch or other additive. Suitable additives are sucrose, lactose, cellulose sugar, mannitol, maltitol, dextran, starch, agar, alginates, chitins, chitosans, pectins, tragacanth gum, gum arabic, gelatins, collagens, casein, albumin, synthetic or semi-synthetic polymers or

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glycerides. Optionally, oral dosage forms can contain other ingredients to aid in administration, such as an inactive diluent, or lubricants such as magnesium stearate, or preservatives such as paraben or sorbic acid, or anti-oxidants such as ascorbic acid, tocopherol or cysteine, a disintegrating agent, binders, thickeners, buffers, sweeteners, flavoring agents or perfuming agents. Tablets and pills may be further treated with suitable coating materials known in the art.

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Liquid dosage forms for oral administration may be in the form of pharmaceutically acceptable emulsions, syrups, elixirs, suspensions, and solutions, which may contain an inactive diluent, such as water. Pharmaceutical formulations and medicaments may be prepared as liquid suspensions or solutions using a sterile liquid, such as, but not limited to, an oil, water, an alcohol, and combinations of these. Pharmaceutically suitable surfactants, suspending agents, emulsifying agents, may be added for oral or parenteral administration.

As noted above, suspensions may include oils. Such oil include, but are not limited to, peanut oil, sesame oil, cottonseed oil, corn oil and olive oil. Suspension preparation may also contain esters of fatty acids such as ethyl oleate, isopropyl myristate, fatty acid glycerides and acetylated fatty acid glycerides. Suspension formulations may include alcohols, such as, but not limited to, ethanol, isopropyl alcohol, hexadecyl alcohol, glycerol and propylene glycol. Ethers, such as but not limited to, poly(ethyleneglycol), petroleum hydrocarbons such as mineral oil and petrolatum; and water may also be used in suspension formulations.

For nasal administration, the pharmaceutical formulations and medicaments may be a spray or aerosol containing an appropriate solvent(s) and optionally other compounds such as, but not limited to, stabilizers, antimicrobial agents, antioxidants, pH modifiers, surfactants, bioavailability modifiers and combinations of these. A propellant for an aerosol formulation may include compressed air, nitrogen, carbon dioxide, or a hydrocarbon based low boiling solvent.

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Injectable dosage forms generally include aqueous suspensions or oil suspensions which may be prepared using a suitable dispersant or wetting agent and a suspending agent. Injectable forms may be in solution phase or in the form of a suspension, which is prepared with a solvent or diluent. Acceptable solvents or vehicles include sterilized water, Ringer's solution, or an isotonic aqueous saline solution. Alternatively, sterile oils may be employed as solvents or suspending agents. Preferably, the oil or fatty acid is non-volatile, including natural or synthetic oils, fatty acids, mono-, di- or tri-glycerides.

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For injection, the pharmaceutical formulation and/or medicament may be a powder suitable for reconstitution with an appropriate solution as described above. Examples of these include, but are not limited to, freeze dried, rotary dried or spray dried powders, amorphous powders, granules, precipitates, or particulates. For injection, the formulations may optionally contain stabilizers, pH modifiers, surfactants, bioavailability modifiers and combinations of these.

For rectal administration, the pharmaceutical formulations and medicaments may be in the form of a suppository, an ointment, an enema, a tablet or a cream for release of compound in the intestines, sigmoid flexure and/or rectum. Rectal suppositories are prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers of the compound, with acceptable vehicles, for example, cocoa butter or polyethylene glycol, which is present in a solid phase at normal storing temperatures, and present in a liquid phase at those temperatures suitable to release a drug inside the body, such as in the rectum. Oils may also be employed in the preparation of formulations of the soft gelatin type and suppositories. Water, saline, aqueous dextrose and related sugar solutions, and glycerols may be employed in the preparation of suspension formulations which may also contain suspending agents such as pectins, carbomers, methyl cellulose, hydroxypropyl cellulose or carboxymethyl cellulose, as well as buffers and preservatives.

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Besides those representative dosage forms described above, pharmaceutically acceptable excipients and carries are generally known to those skilled in the art and are thus included in the instant invention. Such excipients and carriers are described, for example, in "Remingtons Pharmaceutical Sciences" Mack Pub. Co., New Jersey (1991), which is incorporated herein by reference.

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The formulations of the invention may be designed to be short-acting, fast-releasing, long-acting, and sustained-releasing as described below. Thus, the pharmaceutical formulations may also be formulated for controlled release or for slow release.

The instant compositions may also comprise, for example, micelles or liposomes, or some other encapsulated form, or may be administered in an extended release form to provide a prolonged storage and/or delivery effect. Therefore, the pharmaceutical formulations and medicaments may be compressed into pellets or cylinders and implanted intramuscularly or subcutaneously as depot injections or as implants such as stents. Such implants may employ known inert materials such as silicones and biodegradable polymers.

Specific dosages may be adjusted depending on conditions of disease, the age, body weight, general health conditions, sex, and diet of the subject, dose intervals, administration routes, excretion rate, and combinations of drugs. Any of the above dosage forms containing effective amounts are well within the bounds of routine experimentation and therefore, well within the scope of the instant invention.

A therapeutically effective dose may vary depending upon the route of administration and dosage form. The preferred compound or compounds of the instant invention is a formulation that exhibits a high therapeutic index. The therapeutic index is the dose ratio between toxic and therapeutic effects which can be expressed as the ratio between LD50 and ED50. The LD50 is the dose lethal to 50% of the population and the ED50 is the dose therapeutically effective in 50% of

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the population. The LD₅₀ and ED₅₀ are determined by standard pharmaceutical procedures in animal cell cultures or experimental animals.

"Treating" within the context of the instant invention, means an alleviation of symptoms associated with a disorder or disease, or halt of further progression or worsening of those symptoms, or prevention or prophylaxis of the disease or disorder. For example, within the context of treating patients in need of an inhibitor of VEGF-RTK, successful treatment may include a reduction in the proliferation of capillaries feeding a tumor or diseased tissue, an alleviation of symptoms related to a cancerous growth or tumor, proliferation of capillaries, or diseased tissue, a halting in capillary proliferation, or a halting in the progression of a disease such as cancer or in the growth of cancerous cells. Treatment may also include administering the pharmaceutical formulations of the present invention in combination with other therapies. For example, the compounds and pharmaceutical formulations of the present invention may be administered before, during, or after surgical procedure and/or radiation therapy. The compounds of the invention can also be administered in conjunction with other anti-cancer drugs including those used in antisense and gene therapy. Appropriate combinations can be determined by those of skill in the oncology and medicine arts.

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Pharmaceutical formulations and medicaments according to the invention include any of the compounds described above in combination with a pharmaceutically acceptable carrier. Thus, the compounds of the invention may be used to prepare medicaments and pharmaceutical formulations. In some such embodiments, the medicaments and pharmaceutical formulations comprise any of the compounds of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I or pharmaceutically acceptable salts thereof. The invention also provides for the use of any of the compounds of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I or pharmaceutically acceptable salts thereof for the inhibition of an enzyme such as flt-1 (VEGFR1), KDR

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(VEGFR2), Flk-1, bFGFR, GSK-3, CHK-1, NEK-2, cdc 2, or for the treatment of a disease or condition associated with any of these enzymes as described in greater detail below. The invention also provides the use of any of the compounds of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I or pharmaceutically acceptable salts thereof for the manufacture of enzyme inhibition agent such as a tyrosine kinase inhibitor or a serine/threonine kinase inhibitor, a pharmaceutical formulation, or a medicament that inhibits enzymes such as flt-1 (VEGFR1), KDR (VEGFR2), Flk-1, bFGFR, GSK-3, CHK-1, NEK-2, cdc 2, PDGF, and Tie-2 or treats a disease or condition associated with any of these enzymes as described in greater detail below.

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A method of treating a patient in need of an inhibitor of vascular endothelial growth factor receptor tyrosine kinase includes administering an effective amount of a pharmaceutical formulation, a medicament according to the invention or any of the compounds of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I to a patient in need thereof.

A method for inhibiting tumor growth in a patient includes administering an effective amount of the compound, a pharmaceutically acceptable salt thereof of any of the of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I, or a medicament to a patient having a tumor.

A method for inhibiting angiogenesis and tumor growth in a patient includes administering an effective amount of the compound or a pharmaceutically acceptable salt thereof according to a patient in need.

25 The invention provides a method of treating a subject with various tumor types. The method includes administering to the subject, such as a human subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds or a pharmaceutically

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acceptable salt thereof of formula I to the subject. In some such embodiments, the method includes a method of treating a cancer patient.

The invention provides a method of inhibiting an enzyme such as a serine/threonine kinase. The method includes administering to a subject, such as a human subject, a mammalian subject, or a cell subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds or a pharmaceutically acceptable salt thereof of formula I to the subject. In some such embodiments, the serine/threonine kinase is GSK-3. In other such embodiments, the serine/threonine kinase is CHK-1. In other such embodiments, the serine/threonine kinase is NEK-2.

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The invention provides a method of inhibiting an enzyme such as a tyrosine kinase. The method includes administering to a subject, such as a human subject, a mammalian subject, or a cell subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds or a pharmaceutically acceptable salt thereof of formula I to the subject. In some such embodiments, the tyrosine kinase is VEGF.

The invention provides a method of treating a subject with type II diabetes. The method includes administering to the subject, such as a human subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds or a pharmaceutically acceptable salt thereof of formula I to the subject. In some such embodiments, the method includes a method of treating a prediabetic or diabetic patient.

The invention provides a method of stimulating insulin-dependent processes in a patient. The method includes administering to the patient, such as a human patient, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the subject. In some such embodiments, the method includes a method of reducing plasma glucose levels,

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increasing glycogen uptake, potentiating insulin, upregulating glucose synthase activity, and stimulating glycogen synthesis such as in skin, muscle, and fat cells.

The invention provides a method of treating a subject with Alzheimer's disease. The method includes administering to the subject, such as a human subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the subject. In some such embodiments, the method includes reducing tau hyperphosphorylation, reducing the generation of neurofibrillary tangles, and slowing the progression of Alzheimer's disease.

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The invention provides a method of treating a subject with a central nervous system disorder. The method includes administering to the subject, such as a human subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the subject. In some such embodiments, the method includes a method of treating bipolar disorder; increasing the survival of neurons subjected to aberrantly high levels of excitation induced by glutamate; reducing neurodegeneration associated with acute damage such as in cerebral ischemia, traumatic brain injury, and bacterial injury; and reducing chronic neuronal damage associated with Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS associated dementia, amyotrophic lateral sclerosis (AML) and multiple sclerosis.

The invention provides a method of prolonging an immune response in a subject. The method includes administering to the subject, such as a human subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the subject. In some such embodiments, the method includes prolonging and/or potentiating immunostimulatory effects of

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cytokines, and enhancing the potential of cytokines for immunotherapy such as tumor immunotherapy.

The invention provides a method of reducing the splitting of centrosomes in the cells of a subject. The method includes administering to the subject, such as a human subject, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the subject. In some such embodiments, the subject is a cancer patient.

The invention provides a method of blocking DNA repair in a cancer cell of a cancer patient. The method includes administering to the patient, such as a human patient, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the patient..

The invention provides a method of promoting phosphorylation of cdc25 and Wee1 in a patient. The method includes administering to the patient, such as a human patient, a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof, to the patient.

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The invention provides a method of modulating and/or preventing cell cycle arrest in a cell. The method includes contacting the cell with a compound according to any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh group of compounds of formula I, or a pharmaceutically acceptable salt thereof. In one method, the cells are defective in the p53 gene and/or have p53 mutations and/or are deficient in p53. In some embodiments, the cells are cancer cells such as those deficient in p53. In some embodiments, arrest at the G2/M checkpoint is prevented or inhibited. In some embodiments, the method includes treating a patient, such as a human patient with any of the compounds of the invention, and in some such further embodiments, the method further includes

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treating the patient with another therapeutic agent such as a chemotherapeutic agent or with radiation or heat.

A method of preparing pharmaceutical formulations and medicaments includes mixing any of the above-described compounds with a pharmaceutically acceptable carrier.

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The present invention, thus generally described, will be understood more readily by reference to the following examples, which are provided by way of illustration and are not intended to be limiting of the present invention.

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EXAMPLES

Nomenclature for the Example compounds was provided using ACD Name version 5.07 software (November 14, 2001) available from Advanced Chemistry Development, Inc., ChemInnovation NamExpert + NomenclatorTM brand software available from ChemInnovation Software, Inc., and AutoNom version 2.2 available in the ChemOffice® Ultra software package version 7.0 available from CambridgeSoft Corporation (Cambridge, MA). Some of the compounds and starting materials were named using standard IUPAC nomenclature.

The following abbreviations are used throughout the application with

10 respect to chemical terminology:

AcOH:

Acetic acid

ATP:

Adenosine triphosphate

BINAP:

2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl

Boc:

N-tert-Butoxycarbonyl

15 Bn:

Benzyl

BSA:

Bovine Serum Albumin

Cbz:

Carbobenzyloxy

DEAD:

Diethyl azodicarboxylate

DIEA:

Diisopropylethylamine

20 DMA:

N, N-Dimethylacetamide

DMAP:

4-Dimethylaminopyridine

DMF:

N, N-Dimethylformamide

DMSO:

Dimethylsulfoxide

dppf:

1,1'(diphenylphosphino)ferrocene

25 DTT:

DL-Dithiothreitol

ED50:

Dose therapeutically effective in 50% of the population

EDC or EDCI:

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide

hydrochloride

EDTA:

Ethylene diamine tetraacetic acid

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EtOAc:

Ethyl acetate

EtOH:

Ethanol

Fmoc:

9-fluorenylmethyl

HBTU:

O-Benzotriazol-1-yl-N,N,N',N'-tetramethyluronium

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hexafluorophosphate

HPLC:

High Pressure Liquid Chromatography

IC50 value:

The concentration of an inhibitor that causes a 50 % reduction

in a measured activity.

KHMDS:

Potassium bis(trimethylsilyl)amide

10 LC/MS:

Liquid Chromatography/Mass Chromatography

LiHMDS:

Lithium bis(trimethylsilyl)amide

MeOH:

Methanol

NMP:

N-methylpyrrolidone

Pd(dba)2:

Bis(dibenzylideneacetone)Palladium

15 PPTS:

Pyridinium p-toluenesulfonate

Pyr:

Pyridine

SEMCI:

2-(Trimethylsilyl)ethoxymethyl chloride

TBAF:

Tetrabutylammonium fluoride

TEA:

Triethylamine

20 TES:

Triethylsilyl

TFAA:

Trifluoroacetic anhydride

THF:

Tetrahydrofuran

TMS:

Trimethylsilyl

Purification and Characterization of Compounds

25 Compounds of the present invention were characterized by high performance liquid chromatography (HPLC) using a Waters Millenium chromatography system with a 2690 Separation Module (Milford, Massachusetts). The analytical columns were Alltima C-18 reversed phase, 4.6 x 250 mm from Alltech (Deerfield, Illinois). A gradient elution was used, typically starting with 5% acetonitrile/95% water and progressing to 100% acetonitrile over a period of 40 minutes. All solvents contained 0.1% trifluoroacetic acid (TFA). Compounds were

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detected by ultraviolet light (UV) absorption at either 220 or 254 nm. HPLC solvents were from Burdick and Jackson (Muskegan, Michigan), or Fisher Scientific (Pittsburg, Pennsylvania). In some instances, purity was assessed by thin layer chromatography (TLC) using glass or plastic backed silica gel plates, such as, for example, Baker-Flex Silica Gel 1B2-F flexible sheets. TLC results were readily detected visually under ultraviolet light, or by employing well known iodine vapor and other various staining techniques.

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Mass spectrometric analysis was performed on one of two LCMS instruments: a Waters System (Alliance HT HPLC and a Micromass ZQ mass spectrometer; Column: Eclipse XDB-C18, 2.1 x 50 mm; Solvent system: 5-95% acetonitrile in water with 0.05% TFA; Flow rate 0.8 mL/min; Molecular weight range 150-850; Cone Voltage 20 V; Column temperature 40°C) or a Hewlett Packard System (Series 1100 HPLC; Column: Eclipse XDB-C18, 2.1 x 50 mm; Solvent system: 1-95% acetonitrile in water with 0.05% TFA; Flow rate 0.4 mL/min; Molecular weight range 150-850; Cone Voltage 50 V; Column temperature 30°C). All masses are reported as those of the protonated parent ions.

GCMS analysis was performed on a Hewlet Packard instrument (HP6890 Series gas chromatograph with a Mass Selective Detector 5973; Injector volume: 1 μ L; Initial column temperature: 50°C; Final column temperature: 250°C; Ramp time: 20 minutes; Gas flow rate: 1 mL/min; Column: 5% Phenyl Methyl Siloxane, Model #HP 190915-443, Dimensions: 30.0 m x 25 μ m x 0.25 μ m).

Preparative separations were carried out using either a Flash 40 chromatography system and KP-Sil, 60A (Biotage, Charlottesville, Virginia), or by HPLC using a C-18 reversed phase column. Typical solvents employed for the Flash 40 Biotage system were dichloromethane, methanol, ethyl acetate, hexane and triethyl amine. Typical solvents employed for the reverse phase HPLC were varying concentrations of acetonitrile and water with 0.1% trifluoroacetic acid.

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Various functionalized aryl diamines were obtained from commercial sources, prepared by methods know to those of skilled in the art, or were prepared by the following general methods:

METHOD 1

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2,4-Difluoronitrobenzene (1.0 equivalent) was placed in a dry round-bottomed flask equipped with a dry ice condenser charged with acetone and dry ice. Ammonia was condensed into the flask and the resulting solution was stirred at reflux for 7 hours. A yellow precipitate formed within 1 hour. After 7 hours, the condenser was removed and the liquid ammonia was allowed to evaporate over several hours. The crude product was purified by flash chromatography on silica gel (85:15 hexanes:ethyl acetate, product at $R_f = 0.32$, contaminant at $R_f = 0.51$); GC/MS (m/z) 156.1 (M+), R_f 11.16 minutes.

The resulting 5-fluoro-2-nitrophenylamine (1.0 equivalent) and an amine (1.1 equivalents) e.g. N-methyl piperazine, were dissolved in N-methylpyrrolidinone and triethylamine (2.0 equivalents) was added. The reaction mixture was heated at 100°C for 3 hours. The solution was then cooled to room temperature and diluted with water. The resulting precipitate was filtered and dried under vacuum to provide the 2-amino-4-dialkylamino nitrobenzene or 4-dialkylamino nitroaniline. Alternatively, the same product may be obtained by the reaction of commercially available 5-chloro-2-nitrophenylamine (1.0 equivalent) and an amine (5 equivalents; neat). The two are heated at 130°C for 1-2 days and the product is isolated in an identical manner. LC/MS (m/z) 237.1 (MH+), R₁ 1.304 minutes.

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The nitroamine (1.0 equivalent) and 10% Pd/C (0.1 equivalents) were suspended in anhydrous ethanol at room temperature. The reaction flask was evacuated and subsequently filled with H₂. The resulting mixture was then stirred under a hydrogen atmosphere overnight. The resulting solution was filtered through Celite and concentrated under vacuum to provide the crude product which was used without further purification.

METHOD 2

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A round bottom flask was charged with 2,3-difluoro-6-

nitrophenylamine (1 equivalent) and enough NMP to make a viscous slurry. An amine (5 equivalents), e.g. N-methyl piperazine, was added and the solution was heated at 100°C. After 2 hours, the solution was cooled and poured into water. A bright yellow solid formed which was filtered and dried. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS (m/z) 225.1 (MH+), R₁0.335 minutes.

METHOD 3

To a 0.1 M DMF solution of 1,3-difluoro-2-nitrobenzene was added Et₃N (2 equivalents) followed by an amine (1 equivalent), e.g. morpholine. The mixture was stirred for 18 hours and then diluted with water and extracted with ethyl acetate. The combined organic layers were dried over MgSO₄, filtered, and

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concentrated. LC/MS (m/z): 227.2 (MH+), R₁ 2.522 minutes Ammonia was condensed into a bomb containing the crude product. The bomb was sealed and heated to 100°C (over 400 psi). After 72 hours the bomb was allowed to cool and the ammonia was evaporated to provide a reddish solid. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS (m/z) 194.1 (MH+), R₁1.199 minutes.

METHOD 4

$$NH_2$$
 NH_2 NH_2 NH_2

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To a stirred N-methylpyrrolidinone solution containing NaH (1.3 equivalents) was added an alcohol (1.0 equivalent), e.g. 2-methoxyethanol. The resulting mixture was then stirred for 30 minutes. A slurry of 5-fluoro-2-nitrophenylamine in N-methylpyrrolidinone was then added slowly. The mixture was then heated to 100°C. After 2 hours, the reaction mixture was cooled and water was added. The mixture was then filtered and the solid was washed with water and purified by silica gel chromatography (1:1 ethyl acetate:hexane). LC/MS (m/z) 213.2 (MH+), R₁2.24 minutes. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS (m/z) 183.1 (MH+), R₁0.984 minutes.

METHOD 5

$$NH_2$$
 NO_2 NH_2 NH_2 NH_2

Diisopropyl azodicarboxylate (1.1 equivalents) was added dropwise to a stirred solution of 4-amino-3-nitrophenol (1.0 equivalent), triphenylphosphine

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(1.1 equivalents), and an alcohol, e.g. N-(2-hydroxyethyl)morpholine (1.0 equivalent), in tetrahydrofuran at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 hours. The solvent was evaporated, and the product was purified by silica gel chromatography (98:2 CH₂Cl₂:methanol) to yield 4-(2-morpholin-4-ylethoxy)-2-nitrophenylamine as a dark reddish-brown oil. LC/MS (m/z) 268.0 (MH+), R₁ 1.01 minutes. The nitroamine was reduced as in Method 1 to give the crude product which was used without further purification. LC/MS (m/z) 238.3 (MH+), R₁ 0.295 minutes.

METHOD 6

$$NO_2$$
 NH_2 NH_2 NH_2 NH_2 NH_2 NH_2

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To a flask charged with 4-amino-3-nitrophenol (1 equivalent), K₂CO₃ (2 equivalents), and 2-butanone was added an alkyl dibromide, e.g. 1,3-dibromopropane (1.5 equivalents). The resulting mixture was then heated at 80°C for 18 hours. After cooling, the mixture was filtered, concentrated, and diluted with water. The solution was then extracted with CH₂Cl₂ (3 x) and the combined organic layers were concentrated to give a solid that was then washed with pentane. LC/MS (m/z) 275.1 (MH+), R₁2.74 minutes.

An acetonitrile solution of the bromide prepared above, an amine, e.g. pyrrolidine (5 equivalents), Cs₂CO₃ (2 equivalents) and Bu₄NI (0.1 equivalents) was heated at 70°C for 48 hours. The reaction mixture was cooled, filtered, and concentrated. The residue was dissolved in CH₂Cl₂, washed with water, and concentrated to give the desired nitroamine, e.g. 2-nitro-4-(3-pyrrolidin-1-ylpropoxy)phenylamine. LC/MS (m/z) 266.2 (MH+), R₁1.51 minutes. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification.

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METHOD 7

$$NH_2$$
 NO_2
 $NR'R$
 NH_2
 NH_2
 NH_2

To a suspension of 6-chloro-3-nitropyridin-2-amine (1 equivalent) in acetonitrile was added an amine, e.g. morpholine (4 equivalents). The resulting reaction mixture was stirred at 70°C for 5 hours. The solvent was evaporated under reduced pressure, and the residue triturated with ether to provide the desired compound as a bright yellow powder. LC/MS (m/z) 225.0 (MH+), R₁1.79 minutes. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification.

10 METHOD 8

Synthesis of $\{[(5S,2R)-4-(3-Amino-4-nitrophenyl)-5-methylmorpholin-2-yl]methyl<math>\}$ dimethylamine and $\{[(5S,2R)-4-(3,4-diaminophenyl)-5-methylmorpholin-2-yl]methyl<math>\}$ dimethylamine

Step 1. Synthesis of (2S)-[benzylamino]propan-1-ol

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A mixture of (2S)-2-amino propanol (1.2 equivalents), benzaldehyde (1 equivalent), NaHCO₃ (1.5 equivalents) and MeOH, was heated at reflux for 4 hours and then cooled to 0°C. Sodium borohydride (5.0 equivalents)was then added over 1 hour while the reaction was vigorously stirred. The reaction mixture was stirred at room temperature for 4 hours and then filtered over Celite. The filtrate was concentrated, and the residue was dissolved in CH₂Cl₂. The solution was washed successively with water (x2) and brine (x1). The organic extracts were

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collected and dried over Na₂SO₄. The solvent was evaporated to give the desired product as a white solid. GC/MS: 134 (100%, M+-CH₂OH), R_i= 11.57 minutes.

Step 2. Synthesis of (2S,5S)-2-(chloromethyl)-5-methyl-4-benzylmorpholine

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A mixture of (2S)-2-[benzylamino]propan-1-ol (1 equivalent) and epichlorohydrin (1 equivalent) was stirred at room temperature overnight. The mixture was cooled down to 0°C and cold trifluoromethanesulfonic acid (4 equivalents) was added. The flask was equipped with a reflux condenser and the mixture was stirred at 160°C overnight. The reaction mixture was cooled to room temperature, diluted with CH2Cl2 and quenched with ice water. The mixture was then made basic (pH = 12) with a 30% NaOH solution. The two phases were separated, and the aqueous phase was extracted with CH2Cl2. The organic layer was washed with water, brine, dried over Na2SO4 and concentrated to afford a dark brown oil. The crude product contained an equimolar mixture of (2R,5S)-2-(chloromethyl)-5-methyl-4-benzylmorpholine (cis diastereoisomer) and (2S,5S)-2-(chloromethyl)-5-methyl-4-benzylmorpholine (trans diastereoisomer), which were separated by chromatography on silica gel (ethyl acetate/hexanes 1:20 to 1:8). (2S,5S)-2-(chloromethyl)-5-methyl-4-benzyl morpholine was obtained as the isomer with the lower R_f. GC/MS: 239 (15%, M+), $R_i = 15.08$ minutes; LC/MS (m/z): $240.0 \,(MH+), \, R_1 \, 1.56 \, minutes.$

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Step 3. Synthesis of $\{[(5S,2R)-5-methyl-4-benzylmorpholin-2-yl]methyl\}$ -dimethylamine

A mixture of (2S,5S)-2-(chloromethyl)-5-methyl-4-benzylmorpholine

(1 equivalent) and dimethylamine (5 equivalents) in ethanol, was heated at 150°C for 36 hours in a sealed high pressure vessel. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was taken up in 1 N HCl, and the solution was washed with CH₂Cl₂. The water phase was made basic with a 30% aq. NaOH solution (pH=12) and extracted with CH₂Cl₂.

The organic extracts were collected and dried over Na₂SO₄. Evaporation of the solvent under reduced pressure afforded (2S,5S)-2-[dimethylamino(methyl)]-5-methyl-4-benzylmorpholine as a yellow oil. GC/MS: 247 (2%, M-H), 204 (55%, M-NMe₂), R₁= 15.5 min; LC/MS (m/z): 249.2 (MH+), R₁ 0.72 minutes.

Step 4. Synthesis of [((2S,5S)-5-methylmorpholin-2-yl)methyl]dimethylamine

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{[(5S,2R)-5-methyl-4-benzylmorpholin-2-yl]methyl}dimethylamine (1 equivalent), was dissolved in EtOH and the solution was transferred to a stainless steel high pressure vessel equipped with a pressure gauge. 10% Pd/C was added (10 wt.%), and the vessel charged with H₂. The reaction mixture was stirred at

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130°C and 200 psi of H₂ overnight. The reaction mixture was cooled to room temperature, filtered over a pad of Celite, and then evaporated. The desired amine was obtained in quantitative yield as a pale yellow oil. GC/MS: 128 (10%, M+-2xCH₃), 58 (100%, NHCH₂CHO), R₁= 8.16 minutes.

5 Step 5. Synthesis of {[(5S,2R)-4-(3-amino-4-nitrophenyl)-5-methylmorpholin-2-yl]methyl}dimethylamine

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A mixture of 5-fluoro-2-nitroaniline (1.1 equivalents), [((2S,5S)-5-methylmorpholin-2-yl)methyl]dimethylamine (1 equivalent), triethylamine (3 equivalents), and N-methylpyrrolidinone was heated at 140°C for 48 hours in a sealed high pressure vessel. The reaction mixture was then cooled to 25 °C and dissolved in CH₂Cl₂. The solution was washed with water (x2) and dried over Na₂SO₄. Purification *via* chromatography on silica gel (10% MeOH in dichloromethane) afforded the desired product as a dark yellow foam. LC/MS (m/z) 295.2 (MH+) R₁ 1.55 minutes.

Step 6. Synthesis of {[(5S,2R)-4-(3,4-Diaminophenyl)-5-methylmorpholin-2-yl]methyl}dimethylamine

The nitroaniline produced in Step 5 was reduced using the method set forth in Method 1 to provide the crude title compound which was used without further purification.

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METHOD 9

Synthesis of 1,2-diamino-3-methyl-4-fluorobenzene

Step 1. Synthesis of N-(3-fluoro-2-methylphenyl)acetamide

1-amino-3-fluoro-2-methylbenzene (1 equivalent) was dissolved in CH₂Cl₂ and acetic anhydride (2.0 equivalents) was added slowly. The solution was stirred at room temperature for 4 hours. The reaction mixture was then quenched with water, and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with H₂O, a 10% HCl solution, H₂O, and brine. It was then dried over Na₂SO₄ and concentrated *in vacuo*, to yield N-(3-fluoro-2-methylphenyl)acetamide as a pink solid. LC/MS (m/z) 168.2 (MH+), R₁ 1.91 minutes.

Step 2. Synthesis of 1-amino-3-fluoro-2-methyl-6-nitrobenzene

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A mixture of HNO₃/H₂SO₄ (1:1, 60% HNO₃:conc. H₂SO₄) cooled to 0°C was added dropwise to N-(3-fluoro-2-methylphenyl)acetamide to form a 0.16 M solution. The solution was stirred at 0°C for 10 minutes and then at room temperature for 30 minutes. The solution was then diluted with water and made basic (pH=10) by addition of 6 N NaOH. The mixture was then extracted CH₂Cl₂ (3x), dried over Na₂SO₄, and concentrated *in vacuo* to yield 1-amino-3-fluoro-2-methyl-6-nitrobenzene (the acetyl group was removed during basic work up). LC/MS (m/z) 171.1 (MH+), R₄ 1.87 minutes.

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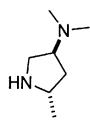
Step 3. Synthesis of 1,2-diamino-4-fluoro-3-methylbenzene

Reduction of the nitro group on 1-amino-3-fluoro-2-methyl-6-nitrobenzene was carried out as described in Method 1 to yield the title compound. LC/MS (m/z) 141.1 (MH+), Rt 0.43 minutes.

METHOD 10

Synthesis of 4-(4-dimethylamino-2-methylpyrrolidin-1-yl)-1,2-diaminobenzene

Step 1. Synthesis of (2S,4S)-4-dimethylamino-2-methylpyrrolidine



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(2S,4S)-4-dimethylamino-2-methylpyrrolidine was synthesized from the Boc-protected cis-4-hydroxy-D-proline methyl ester (available from Bachem) as described in T. Rosen, D.T.W. Chu, I.M. Lico, P.B. Gernandes, K. Marsh, L. Shen, V.G. Cepa, A.G. Pernet, *J. Med. Chem.*, 1988, 31(8), 1598-1611.

Step 2. Synthesis of 3-[(2S,4S)-4-dimethylamino-2-methylpyrrolidin-1-yl]-1-amino-6-nitrobenzene

$$H_2N$$
 O_2N

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(2S,4S)-4-dimethylamino-2-methylpyrrolidine (1.0 equivalent) and 1-amino-3-fluoro-6-nitrobenzene (1.2 equivalents) were dissolved in N-methylpyrrolidinone, and Et3N (5.0 equivalents) was added. The solution was heated for 5 hours at 100°C. The solution was then cooled and diluted with water. The aqueous layer was extracted with ethyl acetate. The organic layer was then washed twice with H₂O, once with brine, dried over Na₂SO₄, filtered, and concentrated. The crude material was purified by column chromatography (1:1 ethyl acetate:hexane to 1:20 MeOH:ethyl acetate to 1:1 MeOH:ethyl acetate to give the title compound as a yellow gum. LC/MS (m/z) 265.2 (MH⁺), R₁ 1.65 minutes.

Step 3. Synthesis of 4-[(2S,4S)-4-dimethylamino-2-methylpyrrolidin-1-yl]-1,2-diaminobenzene

3-[(2S,4S)-4-Dimethylamino-2-methylpyrrolidin-1-yl]-1-amino-6-nitrobenzene was reduced as in Method 1 to afford the title compound. LC/MS (m/z) 235.4 (MH⁺), R_i 0.37 minutes.

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EXAMPLE 1

3-(1H-Benzimidazol-2-yl)-1H-indazole

Synthesis of 11a,5a-Dihydro-1H-indazolo[2',3'-2,1]piperazino[4,5-b]1H-indazole-6,12-dione

Indazole-3-carboxylic acid (1.0 equivalents) was dissolved in phosphorus oxychloride (0.05 equivalents) and refluxed. After 4 hours, the mixture was cooled and concentrated *in vacuo*. The resulting dione was washed three times with benzene, dried, and isolated as a red solid. LC/MS (m/z) 289.1 (MH⁺), R₁ 2.90 minutes.

10 Synthesis of 3-(1H-Benzimidazol-2-yl)-1H-indazole

A toluene solution containing 11a,5a-dihydro-1H-indazolo[2',3'-2,1]piperazino[4,5-b]1H-indazole-6,12-dione (1.0 equivalent) and phenylenediamine (1.5 equivalents), was heated to 100°C. After 18 hours, the solvent was evaporated and the residue was washed repeatedly with water, followed by methanol, and then filtered. Purification by reverse phase preparatory HPLC gave the title compound as a yellow solid. LC/MS (m/z) 235.3 (MH⁺), R₁ 1.90 minutes.

EXAMPLE 2

3-(6-Methoxy-1H-benzimidazol-2-yl)-1H-indazole

Procedure 1

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A solution of 11a,5a-dihydro-1H-indazolo[2',3'-2,1]piperazino[4,5-b]1H-indazole-6,12-dione (1.0 equivalent) from Example 1 and 4-methoxy-ophenylenediamine dihydrochloride (1.5 equivalents) in toluene was heated to 100°C. After 36 hours, the solvent was evaporated and the residue was washed repeatedly with water. The filtrate lyophilized, and the recovered material was purified by

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reverse phase HPLC yielding the title compound as a grey solid. LC/MS (m/z) 265.3 (MH⁺), R₁ 2.04 minutes.

Procedure 2

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A solution containing of 11a,5a-dihydro-1H-indazolo[2',3'2,1]piperazino[4,5-b]1H-indazole-6,12-dione (1.0 equivalent) from Example 1, and
4-methoxy-o-phenylenediamine dihydrochloride (1.5 equivalents) in toluene was
heated at reflux. After two days, the solvent was evaporated and the residue was
washed repeatedly with water. The filtrate was frozen and lyophilized, and the
recovered material was purified by reverse phase HPLC yielding the title compound
as a grey solid. LC/MS (m/z) 265.3 (MH⁺), R₁ 2.04 minutes.

EXAMPLE 3

 $3-\{6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl\}-1H-indazole$ Synthesis of 1H-Indazol-3-yl-N-[5-((6S,2R)-2,6-dimethylmorpholin-4-yl)-2-nitrophenyl] carboxamide

A toluene solution containing 5-[cis-(6S,2R)-2,6-dimethylmorpholin-4-yl)]-2-nitroaniline (2.0 equivalents; synthesized following the procedure described in Method 1 starting from 2,6-cis-dimethylmorpholine and omitting the reduction step), 11a,5a-dihydro-1H-indazolo[2',3'-2,1]piperazino[4,5-b]1H-indazole-6,12-dione from Example 1 (1.0 equivalent), and Et₃N (2.1 equivalents) was heated at reflux for two days. The resulting mixture was then cooled and filtered. The crude material was washed with methanol to provide a brown solid LC/MS (m/z) 396.1 (MH⁺), R₁ 3.44 minutes.

Synthesis of 1H-Indazol-3-yl-N-[5-((6S,2R)-2,6-dimethylmorpholin-4-yl)-2-aminophenyl]carboxamide

To a solution of 1H-indazol-3-yl-N-[5-((6S,2R)-2,6-dimethyl-morpholin-4-yl)-2-nitrophenyl]carboxamide (1.0 equivalent) in ethanol was added

10% Pd/C (0.5 equivalents). The reaction vessel was repeatedly purged with nitrogen, and then the reaction was stirred under a hydrogen atmosphere (1 atm) for 18 hours. The product was filtered through Celite with ethanol. The solvent was removed to provide a brown solid which was used without purification. LC/MS (m/z) 366.2 (MH⁺), R₁ 2.19 minutes.

Synthesis of 3-{6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]-1H-benzimidazol-2- yl}-1H-indazole

1H-Indazol-3-yl-N-[5-((6S,2R)-2,6-dimethyl-morpholin-4-yl)-2-aminophenyl]carboxamide (1.0 equivalent) was dissolved in acetic acid, and sodium acetate (1.1 equivalents) was added. The solution was heated at reflux for 1 hour and then cooled. The acetic acid was removed, and the residue was triturated with ethyl acetate and filtered. The filtrate was concentrated to provide a green foam which was purified by reverse phase HPLC. LC/MS (m/z) 348.1 (MH⁺), R₁ 2.23 minutes.

15 EXAMPLE 4

5-Chloro-3-(5-methyl-1H-benzimidazol-2-yl)-1H-indazole

Procedure 1

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A 0.25 M aqueous solution of NaNO₂ (1.0 equivalent) was brought to a pH of 2.5 by the addition of dilute HCl. Dioxane was added to the solution (10% by volume). The flask was protected from light with aluminum foil and 5-chloroindole (1.0 equivalent) was added slowly. The solution was stirred vigorously for 2 hours. The solution was then extracted with three portions of ethyl acetate. The organic layers were combined, washed with water, dried over MgSO₄, filtered, and concentrated. The product was purified by flash chromatography (ethyl acetate:hexane, 1:1, v/v) yielding 5-chloro-1H-indazole-3-carbaldehyde as a purple solid. LC/MS (m/z) 181.3 (MH+), R₁ 2.7 minutes.

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A flask was charged with 5-chloro-1H-indazole-3-carbaldehyde (1.0 equivalent) and 3,4-diaminotoluene (1.0 equivalent) in toluene and ethanol (approximately 3:1). The flask was heated to 100°C for 18 hours. The solvent was evaporated, and the residue purified by reverse phase HPLC to provide the desired product as a white solid. LC/MS (m/z) 283.1 (MH⁺), R₁ 2.5 minutes.

Procedure 2

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A 0.05 M solution of NaNO₂ (1.0 equivalent) was brought to a pH of 2.5 with the addition of dilute HCl. The flask was protected from light with foil and 5-chloroindole (1.0 equivalent) was added slowly. The solution was left to stir vigorously for 2 hours. The solution was then filtered and extracted with three portions of ethyl acetate. The organic layers were combined, dried over MgSO₄, filtered, and concentrated. The product was purified by flash chromatography (ethyl acetate:hexane, 1:1, v/v) yielding a purple solid. LC/MS (m/z) 181.3 (MH+), R₁ 2.7 minutes.

A flask was charged with 5-chloro-1H-indazole-3-carbaldehyde (1.0 equivalent) and 3,4-diaminotoluene (1.0 equivalent) in toluene and EtOH. The reaction mixture was heated to 100°C for 18 hours. The solvent was then evaporated, and the residue was purified by reverse phase HPLC yielding a white solid. LC/MS (m/z) 283.1 (MH+), R₁ 2.5 minutes.

EXAMPLES 5-670

Examples 5-670 were synthesized following the indole modification and coupling procedure of Example 4. The aryl diamine and the indole precursors are readily recognizable by one skilled in the art and are commercially available from Aldrich (Milwaukee, WI) or Acros Organics (Pittsburgh, PA). 5-Fluoro-6-chloroindole, 6-(trifluoromethyl)indole, 6-nitroindole, and 5-carbethoxyindole may be obtained from Biosynth International (Naperville, IL). 5,6-Difluoroindole and 4,6-difluoroindole may be obtained from Asymchem International, Inc. (Durham, NC). 5,6-Methylenedioxyindole may be obtained from Maybridge Chemical

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Company Ltd. (Cornwall, UK). N-(4-Morpholinoethyl)indole-6-carboxamide may be obtained from Peakdale Molecular (High Peak, UK). The preparation for some of the compounds employed is described in the various methods disclosed herein.

Example	Name	LC/MS (m/z) (MH+)
5	3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	320.1
6	5-chloro-3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl}-1H-indazole	382.1
7	3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl}-5-fluoro-1H-indazole	366.2
8	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-benzimidazol-2-yl}-1H-indazole	347.2
9	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-benzimidazol-2-yl}-5-fluoro-1H-indazole	365.2
10	3-[5-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole	362.3
11	5-fluoro-3-[5-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol- 2-yl]-1H-indazole	380.1
12	6-fluoro-3-[5-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol- 2-yl]-1H-indazole	380.1
13	6-chloro-3-[5-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol- 2-yl]-1H-indazole	396.1
14	3-[5-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole-5-carbonitrile	387.2
15	3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]-1H-indazole	309.2
16	5-fluoro-3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]-1H-indazole	327.2
17	6-fluoro-3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]- 1H-indazole	327.2
18	3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl}-6-fluoro-1H-indazole	366.3
19	6-chloro-3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl}-1H-indazole	382.3

20	ethyl {4-[2-(1H-indazol-3-yl)-1H-benzimidazol-5-yl]piperazin-1-yl}acetate	405.3
21	(3S)-1-[2-(1H-indazol-3-yl)-1H-benzimidazol-5-yl]-N,N-dimethylpyrrolidin-3-amine	347.1
22	2-(1H-indazol-3-yl)-5-morpholin-4-yl-1H-imidazo[4,5-b]pyridine	321.3
23	2-(6-fluoro-1H-indazol-3-yl)-5-morpholin-4-yl-1H-imidazo[4,5-b]pyridine	339.1
24	2-(5-methoxy-1H-indazol-3-yl)-5-morpholin-4-yl-1H-imidazo[4,5-b]pyridine	351.3
25	3-(5-morpholin-4-yl-1H-imidazo[4,5-b]pyridin-2-yl)-1H-indazole-5-carbonitrile	346.3
26	5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1H-indazol-3-yl)-1H-imidazo[4,5-b]pyridine	348.2
27	5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-fluoro-1H-indazol-3-yl)-1H-imidazo[4,5-b]pyridine	366.2
28	5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(5-methoxy-1H-indazol-3-yl)-1H-imidazo[4,5-b]pyridine	378.3
29	3-[6-(pyridin-3-ylmethoxy)-1H-benzimidazol-2-yl]-1H-indazole	342.2
30	6-fluoro-3-[6-(pyridin-3-ylmethoxy)-1H-benzimidazol-2-yl]- 1H-indazole	359.8
31	6-chloro-5-fluoro-3-[6-(pyridin-3-ylmethoxy)-1H-benzimidazol-2-yl]-1H-indazole	393.8
32	4,6-difluoro-3-[6-(pyridin-3-ylmethoxy)-1H-benzimidazol- 2-yl]-1H-indazole	377.9
33	3-[6-(pyridin-3-ylmethoxy)-1H-benzimidazol-2-yl]-1H-indazole-5-carbonitrile	367.1
34	6-fluoro-3-[6-(pyridin-4-ylmethoxy)-1H-benzimidazol-2-yl]-1H-indazole	360.2
35	4,6-difluoro-3-[6-(pyridin-4-ylmethoxy)-1H-benzimidazol- 2-yl]-1H-indazole	377.2
36	1'-[2-(1H-indazol-3-yl)-1H-benzimidazol-6-yl]-1,4'- bipiperidine	401.3
37	1'-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]- 1,4'-bipiperidine	419.3
38	1'-[2-(6-chloro-5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-1,4'-bipiperidine	453.3
39	1'-[2-(4,6-difluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-1,4'-bipiperidine	437.2
40	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	401.3

	1H-indazole	
41	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-fluoro-1H-indazole	419.3
42	6-chloro-3-[6-(4-cyclohexylpiperazin-1-yl)-1H- benzimidazol-2-yl]-5-fluoro-1H-indazole	453.3
43	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]- 4,6-difluoro-1H-indazole	437.2
44	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	361.2
45	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-fluoro-1H-indazole	379.2
46	3-[5-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4,6-difluoro-1H-indazole	397.2
47	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-chloro-5-fluoro-1H-indazole	413.1
48	2-(1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	362.2
49	2-(6-fluoro-1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	379.2
50	2-(4,6-difluoro-1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	397.2
51	2-(6-chloro-5-fluoro-1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	413.2
52	2-(5-fluoro-1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	379.2
53	2-(4-chloro-1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	395.2
54	2-(4-fluoro-1H-indazol-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazol-6-amine	379.3
55	3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	345.2
56	6-fluoro-3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	363.2
57	4,6-difluoro-3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	381.2

58	6-chloro-5-fluoro-3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	397.2
59	5-fluoro-3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	363.2
60	4-chloro-3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	379.2
61	4-fluoro-3-[6-(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)-1H-benzimidazol-2-yl]-1H-indazole	363.2
62	3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	361.3
63	6-fluoro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	379.3
64	6-chloro-5-fluoro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	413.2
65	5-fluoro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	379.3
66	4-fluoro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	395.2
67	4-fluoro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol- 2-yl]-1H-indazole	379.3
68	5,6-difluoro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	397.2
69	4-{[2-(1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	385.1
70	4-{[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	415.2
71	4-{[2-(6-chloro-5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	437.1
72	4-{[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	403.1
73	4-{[2-(4-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	403.1
74	4-{[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	419.1
75	6-methoxy-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	363.1
76	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	333.1

77	5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	367.1
78	5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	351.1
79	5-methoxy-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol- 2-yl]-1H-indazole	363.1
80	2-(1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine	236.1
81	3-[4-chloro-6-(trifluoromethyl)-1H-benzimidazol-2-yl]-1H-indazole	337.1
82	2-(1H-indazol-3-yl)-1H-benzimidazole-6-carboxylic acid	279.1
83	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- nitro-1H-indazole	378.2
84	methyl 3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-5-carboxylate	391.1
85	3-(5-fluoro-6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	338.2
86	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-5-carbonitrile	358.4
87	4,6-difluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	369.1
88	6-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	351.1
89	6-chloro-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	385.1
90	5-chloro-3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]- 1H-indazole	343.2
91	4,6-difluoro-3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]-1H-indazole	345.2
92	6-chloro-5-fluoro-3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]-1H-indazole	361.1
93	3-[5-(2-methoxyethoxy)-1H-benzimidazol-2-yl]-1H-indazole-5-carbonitrile	334.1
94	1-[2-(6-chloro-5-fluoro-1H-indazol-3-yl)-4-methyl-1H-benzimidazol-5-yl]-N,N-dimethylpyrrolidin-3-amine	353.2
95	1-[2-(5-methoxy-1H-indazol-3-yl)-4-methyl-1H-benzimidazol-5-yl]-N,N-dimethylpyrrolidin-3-amine	391.3
96	1-[2-(1H-indazol-3-yl)-4-methyl-1H-benzimidazol-5-yl]- N,N-dimethylpyrrolidin-3-amine	361.3

97	1-[2-(6-chloro-5-fluoro-1H-indazol-3-yl)-4-methyl-1H-benzimidazol-5-yl]-N,N-dimethylpyrrolidin-3-amine	413.2
98	3-(5-morpholin-4-yl-1H-imidazo[4,5-b]pyridin-2-yl)-1H-indazole-5-carboxylic acid	365.2
99	2-(4,6-difluoro-1H-indazol-3-yl)-5-morpholin-4-yl-1H-imidazo[4,5-b]pyridine	357.2
100	2-(6-chloro-5-fluoro-1H-indazol-3-yl)-5-morpholin-4-yl-1H-imidazo[4,5-b]pyridine	373.2
101	ethyl 4-[2-(5,6-difluoro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]piperazine-1-carboxylate	427.2
102	ethyl 4-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]piperazine-1-carboxylate	409.2
103	ethyl 4-[2-(1H-indazol-3-yl)-1H-benzimidazol-5- yl]piperazine-1-carboxylate	391.2
104	ethyl 4-[2-(4-fluoro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]piperazine-1-carboxylate	409.2
105	1'-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-5-yl}-1,4'-bipiperidine	507.4
106	1'-[2-(4-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-yl]- 1,4'-bipiperidine	479.0
107	1'-[2-(5-methyl-1H-indazol-3-yl)-1H-benzimidazol-5-yl]- 1,4'-bipiperidine	415.0
108	1'-[2-(4-fluoro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]- 1,4'-bipiperidine	419.0
109	1'-[2-(4-chloro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]- 1,4'-bipiperidine	435.0
110	1'-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]-1,4'- bipiperidine	446.0
111	3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	351.0
112	4-fluoro-3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	369.0
113	4-chloro-3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	385.0
114	5-fluoro-3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	369.0
115	6-fluoro-3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	369.0
116	3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-(methyloxy)-1H-indazole	381.0
117	6-chloro-5-fluoro-3-[4-fluoro-5-(4-methylpiperazin-1-yl)-	403.0

	1H-benzimidazol-2-yl]-1H-indazole	
118	5,6-difluoro-3-[4-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	387.0
119	4-{[2-(4-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	464.3
120	3-(7-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	320.4
121	4-fluoro-3-(7-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	338.4
122	5-methyl-3-(7-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	334.4
123	5-fluoro-3-(7-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	338.4
124	6-chloro-3-(7-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	354.8
125	5-methoxy-3-(7-morpholin-4-yl-1H-benzimidazol-2-yl)- 1H-indazole	350.4
126	5,6-difluoro-3-(4-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	356.3
127	6-chloro-5-fluoro-3-(4-morpholin-4-yl-1H-benzimidazol- 2-yl)-1H-indazole	372.8
128	2-(1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H- benzimidazol-6-amine	341.4
129	2-(5-methoxy-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)- 1H-benzimidazol-6-amine	371.4
130	2-(6-chloro-5-fluoro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-benzimidazol-6-amine	393.8
131	2-(5-fluoro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-benzimidazol-6-amine	359.4
132	2-(4-bromo-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-benzimidazol-6-amine	420.3
133	2-(4-fluoro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-benzimidazol-6-amine	359.4
134	2-(6-chloro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-benzimidazol-6-amine	375.8
135	2-(1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)-1H- benzimidazol-6-amine	355.4
136	2-(5-methoxy-1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)- 1H-benzimidazol-6-amine	385.4
137	2-(6-chloro-5-fluoro-1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)-1H-benzimidazol-6-amine	407.9
138	2-(5-fluoro-1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)-1H-benzimidazol-6-amine	373.4

2-(4-fluoro-1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)-1H-benzimidazol-6-amine	373.4
2-(6-chloro-1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)-1H- benzimidazol-6-amine	389.9
2-(1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-	341.4
2-(5-methoxy-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-	371.4
2-(6-chloro-5-fluoro-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine	393.8
2-(5-fluoro-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-	359.4
2-(1H-indazol-3-yl)-3H-imidazo[4,5-c]pyridine	236.2
2-(6-chloro-5-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-c]pyridine	288.7
2-(5-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-c]pyridine	254.2
2-(6-chloro-1H-indazol-3-yl)-3H-imidazo[4,5-c]pyridine	270.7
2-(6-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-c]pyridine	254.2
2-(5-chloro-1H-indazol-3-yl)-3H-imidazo[4,5-c]pyridine	270.7
4-fluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole	380.4
5-isopropoxy-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole	420.5
5-methoxy-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-	392.5
5-chloro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-	396.9
4,6-difluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-	398.4
6-chloro-5-fluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-	414.9
3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(2-	557.7
1'-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	446.5
3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-	426.5
INDIALOIC-J-Cai DUITIU IIC	
	2-(6-chloro-1H-indazol-3-yl)-N-(2-pyridin-2-ylethyl)-1H-benzimidazol-6-amine 2-(1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine 2-(5-methoxy-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine 2-(6-chloro-5-fluoro-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine 2-(5-fluoro-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine 2-(1H-indazol-3-yl)-3H-imidazol(4,5-c)pyridine 2-(6-chloro-5-fluoro-1H-indazol-3-yl)-3H-imidazol(4,5-c)pyridine 2-(5-fluoro-1H-indazol-3-yl)-3H-imidazol(4,5-c)pyridine 2-(6-fluoro-1H-indazol-3-yl)-3H-imidazol(4,5-c)pyridine 2-(6-fluoro-1H-indazol-3-yl)-3H-imidazol(4,5-c)pyridine 2-(5-chloro-1H-indazol-3-yl)-3H-imidazol(4,5-c)pyridine 4-fluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole 5-isopropoxy-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole 5-chloro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole 4,6-difluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole 4,6-difluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole 5-chloro-5-fluoro-3-[6-(3-pyrrolidin-1-ylpropoxy)-1H-benzimidazol-2-yl]-1H-indazole 3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(2-morpholin-4-ylethyl)-1H-indazole 3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(2-morpholin-4-ylethyl)-1H-indazole

161	1'-[2-(5-phenoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-1,4'-bipiperidine	493.6
162	2-(4-fluoro-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine	359.4
163	2-(6-chloro-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine	375.8
164	2-(5-isopropoxy-1H-indazol-3-yl)-N-(pyridin-3-ylmethyl)-1H-benzimidazol-6-amine	399.5
165	8-(5-fluoro-1H-indazol-3-yl)-9H-purine	255.2
166	8-(6-fluoro-1H-indazol-3-yl)-9H-purine	255.2
167	6-bromo-2-(5-methoxy-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine	345.2
168	6-bromo-2-(5-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine	333.1
169	6-bromo-2-(4-bromo-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine	394.0
170	8-(6-chloro-1H-indazol-3-yl)-6-methyl-9H-purine	285.7
171	8-(5-isopropoxy-1H-indazol-3-yl)-6-methyl-9H-purine	309.3
172	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}-N'-ethylurea	487.6
173	1'-[2-(1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-5-yl]-1,4'-bipiperidine	402.5
174	1'-[2-(4-bromo-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-5-yl]-1,4'-bipiperidine	481.4
175	1'-[2-(5-chloro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-5-yl]-1,4'-bipiperidine	437.0
176	1'-[2-(5-nitro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-5-yl]-1,4'-bipiperidine	447.5
177	1'-[2-(5-isopropoxy-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-5-yl]-1,4'-bipiperidine	460.6
178	8-(1H-indazol-3-yl)-6-methyl-9H-purine	251.3
179	8-(5-methoxy-1H-indazol-3-yl)-6-methyl-9H-purine	281.3
180	8-(5-fluoro-1H-indazol-3-yl)-6-methyl-9H-purine	269.3
181	3-(5-fluoro-4-methyl-1H-benzimidazol-2-yl)-1H-indazole	267.3
182	3-(5-fluoro-4-methyl-1H-benzimidazol-2-yl)-5-methoxy-1H-indazole	297.3
183	3-(5-fluoro-4-methyl-1H-benzimidazol-2-yl)-N-(2-morpholin-4-ylethyl)-1H-indazole-6-carboxamide	423.5

184	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(5-	538.6
	nitropyridin-2-yl)-1H-indazol-5-amine	
185	1-{1-[2-(1H-indazol-3-yl)-1H-benzimidazol-5-	450.5
	yl]piperidin-4-yl}-1,3-dihydro-2H-benzimidazol-2-one	
186	1-{1-[2-(4-bromo-1H-indazol-3-yl)-1H-benzimidazol-5-	529.4
	yl]piperidin-4-yl}-1,3-dihydro-2H-benzimidazol-2-one	
187	1-{1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-5-	468.5
	yl]piperidin-4-yl}-1,3-dihydro-2H-benzimidazol-2-one	
188	1-{1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-5-	480.5
	yl]piperidin-4-yl}-1,3-dihydro-2H-benzimidazol-2-one	
189	1-{1-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-5-	495.5
	yl]piperidin-4-yl}-1,3-dihydro-2H-benzimidazol-2-one	
190	2-{4-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	381.4
	yl]piperazin-1-yl}ethanol	
191	2-{4-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	393.5
	yl]piperazin-1-yl}ethanol	
192	2-{4-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	397.9
	yl]piperazin-1-yl}ethanol	
193	2-{4-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	408.4
·	yl]piperazin-1-yl}ethanol	
194	methyl 3-{6-[4-(2-hydroxyethyl)piperazin-1-yl]-1H-	421.5
	benzimidazol-2-yl}-1H-indazole-5-carboxylate	
195	2-{4-[2-(5-isopropoxy-1H-indazol-3-yl)-1H-benzimidazol-	421.5
	6-yl]piperazin-1-yl}ethanol	
196	2-{4-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	397.9
	yl]piperazin-1-yl}ethanol	
197	2-{4-[2-(5-ethoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	407.5
	yl]piperazin-1-yl}ethanol	
198	2-{4-[2-(5-phenoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	455.5
	yl]piperazin-1-yl}ethanol	
199	2-{4-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	408.4
	yl]piperazin-1-yl}ethanol	
200	3-{6-[4-(2-hydroxyethyl)piperazin-1-yl]-1H-benzimidazol-	519.6
	2-yl}-N-(2-morpholin-4-ylethyl)-1H-indazole-6-	
	carboxamide	
201	2-(6-chloro-1H-indazol-3-yl)-N-piperidin-3-yl-1H-	367.9
	benzimidazol-6-amine	
202	2-(6-chloro-1H-indazol-3-yl)-N-[(5R)-5-	397.9
	(methoxymethyl)pyrrolidin-3-yl]-1H-benzimidazol-6-	
	amine	
203	6-chloro-3-{5-[(2S)-2-(pyrrolidin-1-ylmethyl)pyrrolidin-1-	421.9
	yl]-1H-benzimidazol-2-yl}-1H-indazole	
204	6-fluoro-3-{5-[(2S)-2-(pyrrolidin-1-ylmethyl)pyrrolidin-1-	405.5
	yl]-1H-benzimidazol-2-yl}-1H-indazole	

205	5-(benzyloxy)-3-{5-[(2S)-2-(pyrrolidin-1-	493.6
	ylmethyl)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-1H- indazole	
206	5-methoxy-3-{5-[(2S)-2-(pyrrolidin-1-ylmethyl)pyrrolidin-	417.5
	1-yl]-1H-benzimidazol-2-yl}-1H-indazole	117.5
207	2-(1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	355.4
	benzimidazol-5-amine	
208	2-(5-fluoro-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	373.4
	benzimidazol-5-amine	
209	2-(5-methoxy-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-	385.4
	1H-benzimidazol-5-amine	
210	2-(5-chloro-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	389.9
	benzimidazol-6-amine	
211	2-(5-nitro-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	400.4
	benzimidazol-6-amine	
212	methyl 3-{6-[(2-pyridin-3-ylethyl)amino]-1H-	413.5
	benzimidazol-2-yl}-1H-indazole-5-carboxylate	
213	2-(5-isopropoxy-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-	413.5
	1H-benzimidazol-6-amine	252 1
214	2-(6-fluoro-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	373.4
015	benzimidazol-6-amine	200.0
215	2-(6-chloro-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-benzimidazol-6-amine	389.9
216	2-(6-methoxy-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-	385.4
210	1H-benzimidazol-6-amine	363.4
217	2-(5-ethoxy-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	399.5
217	benzimidazol-6-amine	377.3
218	2-(5-phenoxy-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-	447.5
0	1H-benzimidazol-6-amine	117.5
219	2-(6-nitro-1H-indazol-3-yl)-N-(2-pyridin-3-ylethyl)-1H-	400.4
	benzimidazol-6-amine	
220	2-(5-chloro-1H-indazol-3-yl)-N-[3-(1H-imidazol-1-	392.9
	yl)propyl]-1H-benzimidazol-6-amine	
221	N-[3-(1H-imidazol-1-yl)propyl]-2-(5-methoxy-1H-indazol-	388.4
	3-yl)-1H-benzimidazol-6-amine	
222	N-[3-(1H-imidazol-1-yl)propyl]-2-(5-nitro-1H-indazol-3-	403.4
	yl)-1H-benzimidazol-6-amine	
223	methyl 3-(6-{[3-(1H-imidazol-1-yl)propyl]amino}-1H-	416.5
	benzimidazol-2-yl)-1H-indazole-5-carboxylate	
224	3-(6-{[3-(1H-imidazol-1-yl)propyl]amino}-1H-	383.4
	benzimidazol-2-yl)-1H-indazole-5-carbonitrile	
225	2-[5-(benzyloxy)-1H-indazol-3-yl]-N-[3-(1H-imidazol-1-	464.5
	yl)propyl]-1H-benzimidazol-6-amine	
226	N-[3-(1H-imidazol-1-yl)propyl]-2-(5-isopropoxy-1H-	416.5
	indazol-3-yl)-1H-benzimidazol-6-amine	

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227	2-(6-fluoro-1H-indazol-3-yl)-N-[3-(1H-imidazol-1-	376.4
	yl)propyl]-1H-benzimidazol-6-amine	
228	2-(6-chloro-1H-indazol-3-yl)-N-[3-(1H-imidazol-1-	392.9
	yl)propyl]-1H-benzimidazol-6-amine	
229	2-(5-ethoxy-1H-indazol-3-yl)-N-[3-(1H-imidazol-1-	402.5
	yl)propyl]-1H-benzimidazol-6-amine	
230	N-[3-(1H-imidazol-1-yl)propyl]-2-(6-nitro-1H-indazol-3-	403.4
	yl)-1H-benzimidazol-6-amine	
231	2-(1H-indazol-3-yl)-N-(2-morpholin-4-ylethyl)-1H-	363.4
	benzimidazol-6-amine	
232	2-(5-chloro-1H-indazol-3-yl)-N-(2-morpholin-4-ylethyl)-	397.9
	1H-benzimidazol-6-amine	
233	2-(5-methoxy-1H-indazol-3-yl)-N-(2-morpholin-4-	393.5
	ylethyl)-1H-benzimidazol-6-amine	
234	2-[5-(benzyloxy)-1H-indazol-3-yl]-N-(2-morpholin-4-	469.6
	ylethyl)-1H-benzimidazol-6-amine	
235	2-(6-fluoro-1H-indazol-3-yl)-N-(2-morpholin-4-ylethyl)-	381.4
	1H-benzimidazol-6-amine	
236	2-(6-chloro-1H-indazol-3-yl)-N-(2-morpholin-4-ylethyl)-	397.9
	1H-benzimidazol-6-amine	
237	2-(5-ethoxy-1H-indazol-3-yl)-N-(2-morpholin-4-ylethyl)-	407.5
	1H-benzimidazol-6-amine	
238	N-(2-morpholin-4-ylethyl)-2-(6-nitro-1H-indazol-3-yl)-	408.4
	1H-benzimidazol-6-amine	
239	5-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H-	395.9
	benzimidazol-2-yl]-1H-indazole	
240	5-bromo-3-[6-(4-isopropylpiperazin-1-yl)-1H-	440.4
	benzimidazol-2-yl]-1H-indazole	
241	3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-	391.5
	methoxy-1H-indazole	
242	3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-	406.5
	nitro-1H-indazole	
243	methyl 3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-	419.5
	2-yl]-1H-indazole-5-carboxylate	
244		
244	5-(benzyloxy)-3-[6-(4-isopropylpiperazin-1-yl)-1H-	467.6
244		467.6
	benzimidazol-2-yl]-1H-indazole	
244	benzimidazol-2-yl]-1H-indazole 6-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H-	395.9
245	benzimidazol-2-yl]-1H-indazole 6-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	395.9
	benzimidazol-2-yl]-1H-indazole 6-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole 3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-	
245 246	benzimidazol-2-yl]-1H-indazole 6-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole 3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6- methoxy-1H-indazole	395.9 391.5
245	benzimidazol-2-yl]-1H-indazole 6-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole 3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6- methoxy-1H-indazole 5-ethoxy-3-[6-(4-isopropylpiperazin-1-yl)-1H-	395.9
245 246	benzimidazol-2-yl]-1H-indazole 6-chloro-3-[6-(4-isopropylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole 3-[6-(4-isopropylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6- methoxy-1H-indazole	395.9 391.5

5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(5-fluoro-1H-	366.4
▼ : =:	382.9
* • • • • • • • • • • • • • • • • • • •	393.4
	382.9
	393.4
2-(5-fluoro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-	408.5
yl)propyl]-1H-benzimidazol-6-amine	
2-(5-chloro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-	424.9
yl)propyl]-1H-benzimidazol-6-amine	
2-(5-bromo-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-	469.4
yl)propyl]-1H-benzimidazol-6-amine	
2-(5-methoxy-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-	420.5
1-yl)propyl]-1H-benzimidazol-6-amine	
N-[3-(4-methylpiperazin-1-yl)propyl]-2-(5-nitro-1H-	435.5
indazol-3-yl)-1H-benzimidazol-6-amine	
methyl 3-(6-{[3-(4-methylpiperazin-1-yl)propyl]amino}-	448.5
1H-benzimidazol-2-yl)-1H-indazole-5-carboxylate	
2-[5-(benzyloxy)-1H-indazol-3-yl]-N-[3-(4-	496.6
methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine	
2-(6-fluoro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-	408.5
yl)propyl]-1H-benzimidazol-6-amine	
2-(6-chloro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-	424.9
yl)propyl]-1H-benzimidazol-6-amine	
	434.6
	435.5
	359.4
	375.8
	2.0,0
	371.4
	0,1
	386.4
	500.1
methyl 3-{6-[(pyridin-2-ylmethyl)amino]-1H-	399.4
i moniji o to tepinom z jimoniji/mimoj iii	U) J . T
henzimidazol-2-vl}-1H-indazole-5-carboxylate	
benzimidazol-2-yl}-1H-indazole-5-carboxylate 2-(6-fluoro-1H-indazol-3-yl)-N-(pyridin-2-ylmethyl)-1H-	359.4
	indazol-3-yl)-3H-imidazo[4,5-b]pyridine 2-(5-chloro-1H-indazol-3-yl)-5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3H-imidazo[4,5-b]pyridine 5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(5-nitro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 2-(6-chloro-1H-indazol-3-yl)-5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3H-imidazo[4,5-b]pyridine 5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-nitro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 2-(5-fluoro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-fluoro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-bromo-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-methoxy-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine N-[3-(4-methylpiperazin-1-yl)propyl]-2-(5-nitro-1H-indazol-3-yl)-1H-indazol-3-yl]-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-fluoro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(6-fluoro-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-ethoxy-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-ethoxy-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-ethoxy-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-ethoxy-1H-indazol-3-yl)-N-[3-(4-methylpiperazin-1-yl)propyl]-1H-benzimidazol-6-amine 2-(5-methoxy-1H-indazol-3-yl)-N-[yyridin-2-ylmethyl)-1H-benzimidazol-6-amine 2-(5-nitro-1H-indazol-3-yl)-N-(pyridin-2-ylmethyl)-1H-benzimidazol-6-amine

271	2-(5-ethoxy-1H-indazol-3-yl)-N-(pyridin-2-ylmethyl)-1H-benzimidazol-6-amine	385.4
272	2-(6-nitro-1H-indazol-3-yl)-N-(pyridin-2-ylmethyl)-1H-benzimidazol-6-amine	386.4
273	2-(5-fluoro-1H-indazol-3-yl)-N-piperidin-3-yl-1H- benzimidazol-5-amine	351.4
274	methyl 3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2-yl]-1H-indazole-5-carboxylate	391.4
275	2-(5,6-difluoro-1H-indazol-3-yl)-N-piperidin-3-yl-1H- benzimidazol-5-amine	369.4
276	3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2-yl]-1H-indazole-6-carbonitrile	358.4
277	2-(6-fluoro-1H-indazol-3-yl)-N-piperidin-3-yl-1H- benzimidazol-5-amine	351.4
278	2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazole-6-carboxylic acid	313.7
279	2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazole-6-carboxylic acid	385.4
280	3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	319.4
281	5-chloro-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	353.8
282	5-bromo-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	398.3
283	5-methoxy-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	349.4
284	5-nitro-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	364.4
285	methyl 3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole-5-carboxylate	377.4
286	5-(benzyloxy)-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	425.5
287	5-isopropoxy-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	377.5
288	6-fluoro-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	337.4
289	6-chloro-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	353.8
290	6-methoxy-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	349.4
291	5-ethoxy-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-indazole	363.4
292	6-nitro-3-(6-piperazin-1-yl-1H-benzimidazol-2-yl)-1H-	364.4

293	2-(5-methyl-1H-indazol-3-yl)-N-piperidin-3-yl-1H-	347.4
	benzimidazol-5-amine	
294	1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	352.4
	yl]piperidin-4-ol	
295	1-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	368.8
	yl]piperidin-4-ol	_
296	1-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-	413.3
	yl]piperidin-4-ol	
297	1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	364.4
	yl]piperidin-4-ol	
298	1-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	379.4
	yl]piperidin-4-ol	
299	methyl 3-[6-(4-hydroxypiperidin-1-yl)-1H-benzimidazol-	392.4
	2-yl]-1H-indazole-5-carboxylate	
300	1-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-6-	440.5
500	yl}piperidin-4-ol	
301	1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	352.4
301	yl]piperidin-4-ol	332.1
302	1-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	368.8
502	yl]piperidin-4-ol	500.0
303	1-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	379.4
303	yl]piperidin-4-ol	517.4
304	2-(5-fluoro-1H-indazol-3-yl)-N-(2-piperidin-1-ylethyl)-	379.5
J04	1H-benzimidazol-6-amine	317.5
305	2-(1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-ylethyl)-1H-	369.4
303	benzimidazol-6-amine	307.4
306	2-(5-fluoro-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	387.4
300	ylethyl)-1H-benzimidazol-6-amine	307.4
307	2-(5-chloro-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	403.9
307	ylethyl)-1H-benzimidazol-6-amine	1 03.7
308	2-(5-methoxy-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	399.5
500	ylethyl)-1H-benzimidazol-6-amine	377.3
309	2-(6-fluoro-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	387.4
309	ylethyl)-1H-benzimidazol-6-amine	307.4
310	2-(6-chloro-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	403.9
310		403.9
211	ylethyl)-1H-benzimidazol-6-amine	399.5
311	2-(6-methoxy-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	399.3
210	ylethyl)-1H-benzimidazol-6-amine	410.5
312	2-(5-ethoxy-1H-indazol-3-yl)-N-methyl-N-(2-pyridin-2-	413.5
212	ylethyl)-1H-benzimidazol-6-amine	414 4
313	N-methyl-2-(6-nitro-1H-indazol-3-yl)-N-(2-pyridin-2-	414.4
	ylethyl)-1H-benzimidazol-6-amine	505.5
314	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	595.7
	1H-indazol-5-yl}-N'-(2,4-dimethoxyphenyl)urea	
315	2-(5-chloro-1H-indazol-3-yl)-N-methyl-N-(1-	395.9

	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
316	2-(5-bromo-1H-indazol-3-yl)-N-methyl-N-(1-	440.4
310	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	7.7
317	2-(5-methoxy-1H-indazol-3-yl)-N-methyl-N-(1-	391.5
317		391.3
210	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	406.5
318	N-methyl-N-(1-methylpiperidin-4-yl)-2-(5-nitro-1H-	400.3
210	indazol-3-yl)-1H-benzimidazol-6-amine	410.6
319	methyl 3-{6-[methyl(1-methylpiperidin-4-yl)amino]-1H-	419.5
	benzimidazol-2-yl}-1H-indazole-5-carboxylate	
320	N-methyl-2-(5-methyl-1H-indazol-3-yl)-N-(1-	375.5
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
321	2-[5-(benzyloxy)-1H-indazol-3-yl]-N-methyl-N-(1-	467.6
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
322	2-(6-chloro-1H-indazol-3-yl)-N-methyl-N-(1-	395.9
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
323	2-(6-methoxy-1H-indazol-3-yl)-N-methyl-N-(1-	391.5
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
324	2-(5-ethoxy-1H-indazol-3-yl)-N-methyl-N-(1-	405.5
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
325	N-methyl-N-(1-methylpiperidin-4-yl)-2-(6-nitro-1H-	406.5
	indazol-3-yl)-1H-benzimidazol-6-amine	
326	2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-N-methyl-N-(1-	405.5
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
327	N-methyl-2-(7-methyl-1H-indazol-3-yl)-N-(1-	375.5
	methylpiperidin-4-yl)-1H-benzimidazol-6-amine	
328	N-(1-benzylpiperidin-4-yl)-2-(5-methoxy-1H-indazol-3-	453.6
,,,,	yl)-1H-benzimidazol-6-amine	
329	N-(1-benzylpiperidin-4-yl)-2-(6-fluoro-1H-indazol-3-yl)-	441.5
J 2 J	1H-benzimidazol-6-amine	
330	2-(6-chloro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-	389.9
550	benzimidazol-5-amine	567.7
331	1-[2-(1H-indazol-3-yl)-1H-benzimidazol-6-yl]piperidin-3-	334.4
JJ1	ol	JJ4.4
332	1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	352.4
JJ4	yl]piperidin-3-ol	332.4
222	1-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	368.8
333	* '	300.8
224	yl]piperidin-3-ol	412.2
334	1-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-	413.3
205	yl]piperidin-3-ol	264.4
335	1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	364.4
	yl]piperidin-3-ol	
336	1-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	379.4
	yl]piperidin-3-ol	
337	methyl 3-[6-(3-hydroxypiperidin-1-yl)-1H-benzimidazol-	392.4
	2-yl]-1H-indazole-5-carboxylate	

338	1-[2-(5-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-	348.4
	yl]piperidin-3-ol	<u> </u>
339	1-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-6-yl}piperidin-3-ol	440.5
340	1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	352.4
340	yl]piperidin-3-ol	332.4
341	1-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	368.8
341	yl]piperidin-3-ol	300.0
342	1-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	364.4
	yl]piperidin-3-ol	
343	1-[2-(5-ethoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	378.4
	yl]piperidin-3-ol	
344	1-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	379.4
	yl]piperidin-3-ol	
345	1-[2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-1H-	378.4
	benzimidazol-6-yl]piperidin-3-ol	
346	1-[2-(7-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-	348.4
	yl]piperidin-3-ol	
347	(3R)-1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	338.4
	yl]pyrrolidin-3-ol	
348	(3R)-1-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	354.8
240	yl]pyrrolidin-3-ol	200.2
349	(3R)-1-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-	399.3
250	yl]pyrrolidin-3-ol	350.4
350	(3R)-1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]pyrrolidin-3-ol	330.4
351	(3R)-1-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	365.4
331	yl]pyrrolidin-3-ol	303.4
352	(3R)-1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	378.4
332	yl]pyrrolidin-3-ol	370.4
353	(3R)-1-[2-(5-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-	334.4
555	yl]pyrrolidin-3-ol	
354	(3R)-1-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-	426.5
	benzimidazol-6-yl}pyrrolidin-3-ol	
355	(3R)-1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	338.4
	yl]pyrrolidin-3-ol	
356	(3R)-1-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	354.8
	yl]pyrrolidin-3-ol	
357	(3R)-1-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzimidazol-	350.4
	6-yl]pyrrolidin-3-ol	
358	(3R)-1-[2-(5-ethoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	364.4
	yl]pyrrolidin-3-ol	
359	(3R)-1-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	365.4
	yl]pyrrolidin-3-ol	
360	(3R)-1-[2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-1H-	364.4

	benzimidazol-6-yl]pyrrolidin-3-ol	
361	(3R)-1-[2-(7-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-	334.4
	yl]pyrrolidin-3-ol	
362	6-fluoro-3-{6-[(4-methylpiperazin-1-yl)carbonyl]-1H-	379.4
	benzimidazol-2-yl}-1H-indazole	
363	1'-{[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	447.5
	yl]carbonyl}-1,4'-bipiperidine	
364	6-fluoro-3-[6-(morpholin-4-ylcarbonyl)-1H-benzimidazol-	366.4
	2-yl]-1H-indazole	
365	2-(6-fluoro-1H-indazol-3-yl)-N-methyl-N-(1-	407.5
	methylpiperidin-4-yl)-1H-benzimidazole-6-carboxamide	
366	3-(6-{[(2R,6S)-2,6-dimethylmorpholin-4-yl]carbonyl}-1H-	394.4
	benzimidazol-2-yl)-6-fluoro-1H-indazole	
367	2-(6-fluoro-1H-indazol-3-yl)-N-methyl-N-(1-	393.4
	methylpyrrolidin-3-yl)-1H-benzimidazole-6-carboxamide	
368	(3S,5S)-1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-	379.5
	5-yl]-N,N,5-trimethylpyrrolidin-3-amine	
369	1-[2-(1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	410.5
	phenylpiperidin-4-ol	
370	1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	428.5
	phenylpiperidin-4-ol	
371	1-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	444.9
	phenylpiperidin-4-ol	
372	1-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	489.4
	phenylpiperidin-4-ol	
373	1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	440.5
	4-phenylpiperidin-4-ol	
374	1-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	455.5
	phenylpiperidin-4-ol	
375	methyl 3-[6-(4-hydroxy-4-phenylpiperidin-1-yl)-1H-	468.5
	benzimidazol-2-yl]-1H-indazole-5-carboxylate	
376	1-[2-(5-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	424.5
	phenylpiperidin-4-ol	
377	1-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-6-	516.6
	yl}-4-phenylpiperidin-4-ol	
3,78	1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	428.5
•	phenylpiperidin-4-ol	
379	1-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	444.9
	phenylpiperidin-4-ol	
380	1-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	440.5
	4-phenylpiperidin-4-ol	
381	1-[2-(5-ethoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	454.5
	phenylpiperidin-4-ol	
382	1-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	455.5
	phenylpiperidin-4-ol	

383	1-[2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-1H-	454.5
	benzimidazol-6-yl]-4-phenylpiperidin-4-ol	
384	1-[2-(7-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	424.5
	phenylpiperidin-4-ol	
385	1-[2-(7-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-4-	444.9
	phenylpiperidin-4-ol	
386	1-[2-(1H-indazol-3-yl)-1H-benzimidazol-6-yl]-N,N-	347.4
	dimethylpyrrolidin-3-amine	
387	1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	365.4
	N,N-dimethylpyrrolidin-3-amine	
388	1-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	381.9
	N,N-dimethylpyrrolidin-3-amine	·
389	1-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	426.3
	N,N-dimethylpyrrolidin-3-amine	
390	1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	377.5
	N,N-dimethylpyrrolidin-3-amine	
391	N,N-dimethyl-1-[2-(5-nitro-1H-indazol-3-yl)-1H-	392.4
	benzimidazol-6-yl]pyrrolidin-3-amine	
392	methyl 3-{6-[3-(dimethylamino)pyrrolidin-1-yl]-1H-	405.5
	benzimidazol-2-yl}-1H-indazole-5-carboxylate	
393	1-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-6-	453.6
	yl}-N,N-dimethylpyrrolidin-3-amine	·
394	1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	365.4
	N,N-dimethylpyrrolidin-3-amine	
395	1-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	381.9
	N,N-dimethylpyrrolidin-3-amine	
396	1-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	377.5
	N,N-dimethylpyrrolidin-3-amine	
397	1-[2-(5-ethoxy-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	391.5
	N,N-dimethylpyrrolidin-3-amine	
. 398	N,N-dimethyl-1-[2-(6-nitro-1H-indazol-3-yl)-1H-	392.4
	benzimidazol-6-yl]pyrrolidin-3-amine	
399	N,N-dimethyl-1-[2-(7-methyl-1H-indazol-3-yl)-1H-	361.5
	benzimidazol-6-yl]pyrrolidin-3-amine	
400	1-[2-(7-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	381.9
	N,N-dimethylpyrrolidin-3-amine	
401	5-fluoro-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-	338.4
	indazole	
402	5-chloro-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-	354.8
	indazole	
403	5-bromo-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-	399.3
i	indazole	
404	5-methoxy-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-	350.4
.==	1H-indazole	0.65 1
405	3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-5-nitro-1H-	365.4

	indazole	
406	methyl 3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole-5-carboxylate	378.4
407	5-methyl-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	334.4
408	5-(benzyloxy)-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	426.5
409	6-fluoro-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	338.4
410	6-chloro-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	354.8
411	6-methoxy-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)- 1H-indazole	350.4
412	5-ethoxy-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	364.4
413	3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-6-nitro-1H-indazole	365.4
414	3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H- [1,3]dioxolo[4,5-f]indazole	364.4
415	7-methyl-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	334.4
416	7-chloro-3-(6-morpholin-4-yl-1H-benzimidazol-2-yl)-1H-indazole	354.8
417	N-({(2R,5S)-4-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-5-yl]-5-methylmorpholin-2-yl}methyl)-N,N-dimethylamine	425.9
418	N-(3,4-dimethoxybenzyl)-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-amine	498.6
419	N-[4-(benzyloxy)-3-methoxybenzyl]-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-amine	574.7
420	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N- (4-phenoxybenzyl)-1H-indazol-5-amine	530.6
421	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-fluoro-1H-indazole	379.4
422	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-chloro-1H-indazole	395.9
423	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- bromo-1H-indazole	440.3
424	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- nitro-1H-indazole	406.4
425	methyl 3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-5-carboxylate	419.5
426	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- methyl-1H-indazole	375.4

427	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- (benzyloxy)-1H-indazole	467.5
428	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-chloro-1H-indazole	395.9
429	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6- methoxy-1H-indazole	391.4
430	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- ethoxy-1H-indazole	405.5
431	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6- nitro-1H-indazole	406.4
432	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H- [1,3]dioxolo[4,5-f]indazole	405.4
433	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-7- methyl-1H-indazole	375.4
434	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-7-chloro-1H-indazole	395.9
435	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-[(2-chloropyridin-3-yl)methyl]-1H-indazol-5-amine	542.1
436	2-(5-fluoro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	373.4
437	2-(5-chloro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	389.9
438	2-(5-methoxy-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)- 1H-benzimidazol-6-amine	385.4
439	2-(5-nitro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	400.4
440	methyl 3-{6-[(2-pyridin-4-ylethyl)amino]-1H- benzimidazol-2-yl}-1H-indazole-5-carboxylate	413.5
441	2-(6-fluoro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	373.4
442	2-(6-chloro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	389.9
443	2-(6-methoxy-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)- 1H-benzimidazol-6-amine	385.4
444	2-(5-ethoxy-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	399.5
445	2-(6-nitro-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H- benzimidazol-6-amine	400.4
446	2-(5-methyl-1H-indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	369.4
447	2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-N-(2-pyridin-4-ylethyl)-1H-benzimidazol-6-amine	399.4
448	2-(5-methyl-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)- 1H-benzimidazol-6-amine	389.9
449	2-(1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-1H-	377.5

	7	·
	benzimidazol-6-amine	
450	2-(5-fluoro-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	395.5
	1H-benzimidazol-6-amine	
451	2-(5-chloro-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	411.9
	1H-benzimidazol-6-amine	
452	2-(5-bromo-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	456.4
	1H-benzimidazol-6-amine	
453	2-(5-methoxy-1H-indazol-3-yl)-N-(3-morpholin-4-	407.5
	ylpropyl)-1H-benzimidazol-6-amine	
454	N-(3-morpholin-4-ylpropyl)-2-(5-nitro-1H-indazol-3-yl)-	422.5
	1H-benzimidazol-6-amine	
455	methyl 3-{6-[(3-morpholin-4-ylpropyl)amino]-1H-	435.5
	benzimidazol-2-yl}-1H-indazole-5-carboxylate	
456	2-(5-methyl-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	391.5
	1H-benzimidazol-6-amine	
457	2-[5-(benzyloxy)-1H-indazol-3-yl]-N-(3-morpholin-4-	483.6
	ylpropyl)-1H-benzimidazol-6-amine	
458	2-(6-fluoro-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	395.5
	1H-benzimidazol-6-amine	
459	2-(6-chloro-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	411.9
	1H-benzimidazol-6-amine	
460	2-(6-methoxy-1H-indazol-3-yl)-N-(3-morpholin-4-	407.5
	ylpropyl)-1H-benzimidazol-6-amine	
461	2-(5-ethoxy-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	421.5
	1H-benzimidazol-6-amine	
462	N-(3-morpholin-4-ylpropyl)-2-(6-nitro-1H-indazol-3-yl)-	422.5
	1H-benzimidazol-6-amine	
463	2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-N-(3-morpholin-4-	421.5
	ylpropyl)-1H-benzimidazol-6-amine	
464	2-(7-chloro-1H-indazol-3-yl)-N-(3-morpholin-4-ylpropyl)-	411.9
	1H-benzimidazol-6-amine	
465	N-(3-morpholin-4-ylpropyl)-2-[6-(trifluoromethyl)-1H-	445.5
	indazol-3-yl]-1H-benzimidazol-6-amine	
466	3,5-bis(1H-benzimidazol-2-yl)-1H-indazole	351.4
467	{1-[2-(1H-indazol-3-yl)-1H-benzimidazol-6-yl]piperidin-	348.4
	4-yl}methanol	
468	{1-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	366.4
	yl]piperidin-4-yl}methanol	
469	{1-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	382.9
	yl]piperidin-4-yl}methanol	
470	{1-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-	427.3
	yl]piperidin-4-yl}methanol	
471	{1-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	378.4
	yl]piperidin-4-yl}methanol	
472	{1-[2-(5-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	393.4

	yl]piperidin-4-yl}methanol	l
473	methyl 3-{6-[4-(hydroxymethyl)piperidin-1-yl]-1H-	406.5
	benzimidazol-2-yl}-1H-indazole-5-carboxylate	
474	{1-[2-(5-methyl-1H-indazol-3-yl)-1H-benzimidazol-6-	362.4
	yl]piperidin-4-yl}methanol	
475	(1-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-	454.5
	6-yl}piperidin-4-yl)methanol	
476	{1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	366.4
	yl]piperidin-4-yl}methanol	
477	{1-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	382.9
	yl]piperidin-4-yl}methanol	
478	{1-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	378.4
	yl]piperidin-4-yl}methanol	
479	{1-[2-(5-ethoxy-1H-indazol-3-yl)-1H-benzimidazol-6-	392.5
	yl]piperidin-4-yl}methanol	
480	{1-[2-(6-nitro-1H-indazol-3-yl)-1H-benzimidazol-6-	393.4
	yl]piperidin-4-yl}methanol	
481	{1-[2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-1H-	392.4
	benzimidazol-6-yl]piperidin-4-yl}methanol	
482	{1-[2-(7-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	382.9
	yl]piperidin-4-yl}methanol	
483	(1-{2-[6-(trifluoromethyl)-1H-indazol-3-yl]-1H-	416.4
	benzimidazol-6-yl}piperidin-4-yl)methanol	
484	3-(1H-benzimidazol-2-yl)-5-(benzyloxy)-1H-indazole	341.4
485	5-(1H-benzimidazol-2-yl)-3-[5-(4-methylpiperazin-1-yl)-	449.5
	1H-benzimidazol-2-yl]-1H-indazole	
486	N-({1-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	379.5
	yl]pyrrolidin-3-yl}methyl)-N,N-dimethylamine	
487	3-(1H-benzimidazol-2-yl)-1H-[1,3]dioxolo[4,5-f]indazole	279.3
488	3-(1H-benzimidazol-2-yl)-6-chloro-1H-indazole	269.7
489	3-(1H-benzimidazol-2-yl)-6-fluoro-1H-indazole	253.3
490	3-(1H-benzimidazol-2-yl)-1H-indazole-6-carbonitrile	260.3
491	3-(1H-benzimidazol-2-yl)-6-nitro-1H-indazole	280.3
492	3-(1H-benzimidazol-2-yl)-N-(2-morpholin-4-ylethyl)-1H-	391.4
	indazole-6-carboxamide	
493	6-fluoro-3-{6-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-	377.4
	2(1H)-yl]-1H-benzimidazol-2-yl}-1H-indazole	
494	5-chloro-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	381.9
	benzimidazol-2-yl}-1H-indazole	
495	5-bromo-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	426.3
	benzimidazol-2-yl}-1H-indazole	
496	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	377.5
	benzimidazol-2-yl}-5-methoxy-1H-indazole	
497	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	392.4
	benzimidazol-2-yl}-5-nitro-1H-indazole	

498	methyl 3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	405.5
490	benzimidazol-2-yl}-1H-indazole-5-carboxylate	403.3
499	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	361.5
499		301.3
500	benzimidazol-2-yl}-5-methyl-1H-indazole	152 6
500	5-(benzyloxy)-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-	453.6
501	1H-benzimidazol-2-yl}-1H-indazole	265.4
501	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	365.4
	benzimidazol-2-yl}-6-fluoro-1H-indazole	
502	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	381.9
	benzimidazol-2-yl}-6-nitro-1H-indazole	
503	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	377.5
	benzimidazol-2-yl}-6-methoxy-1H-indazole	
504	5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1H-pyrazol-3-	297.4
	yl)-1H-benzimidazole	···
505	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	391.5
	benzimidazol-2-yl}-5-ethoxy-1H-indazole	
506	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	392.4
	benzimidazol-2-yl}-6-nitro-1H-indazole	_ •
507	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	391.4
	benzimidazol-2-yl}-1H-[1,3]dioxolo[4,5-f]indazole	
508	7-chloro-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	381.9
	benzimidazol-2-yl}-1H-indazole	
509	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	391.5
	benzimidazol-2-yl}-5-methoxy-4-methyl-1H-indazole	
510	3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-	372.4
	benzimidazol-2-yl}-1H-indazole-6-carbonitrile	
511	5-fluoro-3-(5-methyl-1H-benzimidazol-2-yl)-1H-indazole	267.3
512	5-methoxy-3-(5-methyl-1H-benzimidazol-2-yl)-1H-	279.3
312	indazole	217.5
513	methyl 3-(5-methyl-1H-benzimidazol-2-yl)-1H-indazole-5-	307.3
515	carboxylate	507.5
514	3-(5-methyl-1H-benzimidazol-2-yl)-1H-indazole-5-	274.3
314	carbonitrile	217.3
515	3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-	347.4
313	1H-indazole	J47.4
516	5-fluoro-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	365.4
516		303.4
615	benzimidazol-2-yl]-1H-indazole	201.0
517	5-chloro-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	381.9
510	benzimidazol-2-yl]-1H-indazole	106.0
518	5-bromo-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	426.3
	benzimidazol-2-yl]-1H-indazole	
519	5-methoxy-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	377.5
	benzimidazol-2-yl]-1H-indazole	
520	3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-	392.4
	5-nitro-1H-indazole	

521	methyl 3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	405.5
	benzimidazol-2-yl]-1H-indazole-5-carboxylate	244 -
522	5-methyl-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	361.5
		450.6
523	5-(benzyloxy)-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	453.6
50.4	benzimidazol-2-yl]-1H-indazole	265.4
524	6-fluoro-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	365.4
505		201.0
525	6-chloro-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	381.9
526	6-methoxy-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	377.5
320	benzimidazol-2-yl]-1H-indazole	311.3
507		201.5
527	5-ethoxy-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	391.5
500	benzimidazol-2-yl]-1H-indazole	202.4
528	3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-	392.4
	6-nitro-1H-indazole	
529	3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-	391.4
	1H-[1,3]dioxolo[4,5-f]indazole	
530	7-chloro-3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-	381.9
	benzimidazol-2-yl]-1H-indazole	
531	3-[6-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]-	372.4
	1H-indazole-6-carbonitrile	
532	5-(benzyloxy)-3-[6-(4-methylpiperazin-1-yl)-1H-	439.5
	benzimidazol-2-yl]-1H-indazole	
533	5-isopropoxy-3-[6-(4-methylpiperazin-1-yl)-1H-	391.5
	benzimidazol-2-yl]-1H-indazole	
534	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-	471.5
	[(5-nitropyridin-2-yl)oxy]-1H-indazole	
535	5-methyl-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-	347.4
	2-yl]-1H-indazole	
536	5-ethoxy-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-	377.5
	2-yl]-1H-indazole	
537	5-isobutoxy-3-[6-(4-methylpiperazin-1-yl)-1H-	405.5
	benzimidazol-2-yl]-1H-indazole	
538	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-	378.4
	nitro-1H-indazole	
539	N-isopropyl-3-[6-(4-methylpiperazin-1-yl)-1H-	390.5
	benzimidazol-2-yl]-1H-indazol-6-amine	
540	5-bromo-3-(5-methyl-1H-benzimidazol-2-yl)-1H-indazole	328.2
541	3-(1H-benzimidazol-2-yl)-5-nitro-1H-indazole	280.3
542	methyl 3-(1H-benzimidazol-2-yl)-1H-indazole-5-	293.3
•	carboxylate	
543	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-	367.9
	2-yl]-1H-indazole	
544	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-	378.4

	nitro-1H-indazole	
545	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-6-carbonitrile	358.4
546	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-6-carboxylic acid	377.4
547	3-(1H-benzimidazol-2-yl)-6-methyl-1H-indazole	249.3
548	5-methyl-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-	347.4
	2-yl]-1H-indazole	
549	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-	377.4
550	[1,3]dioxolo[4,5-f]indazole	250.2
550 551	3-(1H-benzimidazol-2-yl)-1H-indazol-6-amine 3-(1H-benzimidazol-2-yl)-1H-indazole-6-carboxylic acid	250.3 279.3
552	· 	265.3
	3-(1H-benzimidazol-2-yl)-6-methoxy-1H-indazole	
553	3-(1H-benzimidazol-2-yl)-1H-indazole-5-carboxylic acid	279.3
554	3-(1H-benzimidazol-2-yl)-5-chloro-1H-indazole	269.7
555	3-(5-chloro-1H-benzimidazol-2-yl)-5-fluoro-1H-indazole	287.7
556	3-(5-chloro-1H-benzimidazol-2-yl)-5-methoxy-1H-indazole	299.7
557	3-(1H-benzimidazol-2-yl)-5-bromo-1H-indazole	314.2
558	3-(1H-benzimidazol-2-yl)-5-fluoro-1H-indazole	253.3
559	3-(1H-benzimidazol-2-yl)-1H-indazole-5-carbonitrile	260.3
560	6-bromo-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol- 2-yl]-1H-indazole	412.3
561	5-bromo-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol- 2-yl]-1H-indazole	412.3
562	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	347.4
563	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-fluoro-1H-indazole	365.4
564	5-chloro-3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	381.9
565	5-bromo-3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	426.3
566	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- methoxy-1H-indazole	377.5
567	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- nitro-1H-indazole	392.4
568	methyl 3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-5-carboxylate	405.5
569	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5- methyl-1H-indazole	361.5
570	5-(benzyloxy)-3-[6-(4-ethylpiperazin-1-yl)-1H-	453.6
	benzimidazol-2-yl]-1H-indazole	

	fluoro-1H-indazole	
572	6-chloro-3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-	381.9
	yl]-1H-indazole	
573	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-	377.5
	methoxy-1H-indazole	
574	5-ethoxy-3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-	391.5
	yl]-1H-indazole	
575	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-	392.4
	nitro-1H-indazole	
576	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-	391.4
	[1,3]dioxolo[4,5-f]indazole	
577	7-chloro-3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-	381.9
	yl]-1H-indazole	
578	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-	391.5
	methoxy-4-methyl-1H-indazole	
579	3-[6-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-	372.4
	indazole-6-carbonitrile	
580	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	419.5
	5-fluoro-1H-indazole	
581	5-chloro-3-[6-(4-cyclohexylpiperazin-1-yl)-1H-	436.0
	benzimidazol-2-yl]-1H-indazole	
582	5-bromo-3-[6-(4-cyclohexylpiperazin-1-yl)-1H-	480.4
	benzimidazol-2-yl]-1H-indazole	
583	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	431.6
	5-methoxy-1H-indazole	
584	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	446.5
	5-nitro-1H-indazole	
585	methyl 3-[6-(4-cyclohexylpiperazin-1-yl)-1H-	459.6
	benzimidazol-2-yl]-1H-indazole-5-carboxylate	
586	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	415.6
	5-methyl-1H-indazole	
587	5-(benzyloxy)-3-[6-(4-cyclohexylpiperazin-1-yl)-1H-	507.7
	benzimidazol-2-yl]-1H-indazole	
588	6-chloro-3-[6-(4-cyclohexylpiperazin-1-yl)-1H-	436.0
	benzimidazol-2-yl]-1H-indazole	
589	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	431.6
	6-methoxy-1H-indazole	
590	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	445.6
	5-ethoxy-1H-indazole	
591	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	446.5
	6-nitro-1H-indazole	
592	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-	445.5
	1H-[1,3]dioxolo[4,5-f]indazole	
593	7-chloro-3-[6-(4-cyclohexylpiperazin-1-yl)-1H-	436.0
	benzimidazol-2-yl]-1H-indazole	.50.0

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594	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-5-methoxy-4-methyl-1H-indazole	445.6
595	3-[6-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-6-carbonitrile	426.5
596	3-(5-chloro-1H-benzimidazol-2-yl)-5-nitro-1H-indazole	314.7
597	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-5-carboxylic acid	377.4
598	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-nitro-1H-indazole	378.4
599	3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	396.5
600	5-fluoro-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole	414.5
601	5-chloro-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	430.9
602	5-bromo-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	475.4
603	5-methoxy-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	426.5
604	5-nitro-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole	441.5
605	methyl 3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole-5-carboxylate	454.5
606	5-methyl-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	410.5
607	5-(benzyloxy)-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	502.6
608	6-fluoro-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole	414.5
609	6-chloro-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole	430.9
610	5-ethoxy-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole	440.5
611	3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-[1,3]dioxolo[4,5-f]indazole	440.5
612	7-chloro-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazole	430.9
613	3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-6-carbonitrile	421.5
614	3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N- [(2S)-pyrrolidin-2-ylmethyl]-1H-indazol-4-amine	431.6
615	3-(6-chloro-1H-benzimidazol-2-yl)-1H-indazole-5- carbonitrile	294.7
616	methyl 3-(6-chloro-1H-benzimidazol-2-yl)-1H-indazole-5-carboxylate	327.7

617	N'-[3-(1H-benzimidazol-2-yl)-1H-indazol-5-yl]-N,N-	335.4
	dimethylpropane-1,3-diamine	
618	5-chloro-3-(6-chloro-1H-benzimidazol-2-yl)-1H-indazole	304.2
619	5-bromo-3-(5-chloro-1H-benzimidazol-2-yl)-1H-indazole	348.6
620	N-({4-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	411.9
	yl]morpholin-2-yl}methyl)-N,N-dimethylamine	:
621	N-({4-[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-	456.4
	yl]morpholin-2-yl}methyl)-N,N-dimethylamine	
622	N,N-dimethyl-N-({4-[2-(5-nitro-1H-indazol-3-yl)-1H-	422.5
	benzimidazol-6-yl]morpholin-2-yl}methyl)amine	
623	methyl 3-(6-{2-[(dimethylamino)methyl]morpholin-4-yl}-	435.5
	1H-benzimidazol-2-yl)-1H-indazole-5-carboxylate	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
624	N-[(4-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-	483.6
02.	benzimidazol-6-yl}morpholin-2-yl)methyl]-N,N-	.02.0
	dimethylamine	
625	N-({4-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	395.5
020	yl]morpholin-2-yl}methyl)-N,N-dimethylamine	0,0.0
626	N-({4-[2-(6-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-	411.9
020	yl]morpholin-2-yl}methyl)-N,N-dimethylamine	411.7
627	3-(6-{2-[(dimethylamino)methyl]morpholin-4-yl}-1H-	402.5
027	benzimidazol-2-yl)-1H-indazole-6-carbonitrile	402.5
628	2-(5-chloro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-	375.8
020	benzimidazol-6-amine	5.5.0
629	2-(5-bromo-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-	MW!
	benzimidazol-6-amine	
630	2-(5-nitro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-	386.4
	benzimidazol-6-amine	
631	2-(5-methyl-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-	355.4
	benzimidazol-6-amine	
632	2-[5-(benzyloxy)-1H-indazol-3-yl]-N-(pyridin-4-	447.5
	ylmethyl)-1H-benzimidazol-6-amine	
633	2-(6-fluoro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-	359.4
	benzimidazol-6-amine	
634	2-(7-chloro-1H-indazol-3-yl)-N-(pyridin-4-ylmethyl)-1H-	375.8
	benzimidazol-6-amine	
635	3-{6-[(pyridin-4-ylmethyl)amino]-1H-benzimidazol-2-yl}-	366.4
	1H-indazole-6-carbonitrile	
636	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-	348.4
	indazol-4-amine	
637	N-({(2S,5S)-4-[2-(6-fluoro-1H-indazol-3-yl)-1H-	409.5
	benzimidazol-6-yl]-5-methylmorpholin-2-yl}methyl)-N,N-	
	dimethylamine	
638	N-({(2S,5S)-4-[2-(6-chloro-1H-indazol-3-yl)-1H-	425.9
220	benzimidazol-6-yl]-5-methylmorpholin-2-yl}methyl)-N,N-	
	dimethylamine	
	*	

639	3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	301.3
640	5-fluoro-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	319.3
641	5-chloro-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	335.8
642	5-bromo-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	380.2
643	3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-5- methoxy-1H-indazole	331.4
644	3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-5-nitro- 1H-indazole	346.3
645	methyl 3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]- 1H-indazole-5-carboxylate	359.4
646	3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-5-methyl-1H-indazole	315.4
647	5-(benzyloxy)-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	407.4
648	6-fluoro-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	319.3
649	6-chloro-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	335.8
650	5-ethoxy-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	345.4
651	3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H- [1,3]dioxolo[4,5-f]indazole	345.3
652	7-chloro-3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole	335.8
653	3-[6-(1H-imidazol-1-yl)-1H-benzimidazol-2-yl]-1H-indazole-6-carbonitrile	326.3
654	2-(5-fluoro-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)- 1H-benzimidazol-6-amine	379.5
655	2-(5-chloro-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)- 1H-benzimidazol-6-amine	395.9
656	2-(5-methoxy-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)-1H-benzimidazol-6-amine	391.5
657	2-(5-nitro-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)- 1H-benzimidazol-6-amine	406.5
658	2-(5-methyl-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)- 1H-benzimidazol-6-amine	375.5
659	2-[5-(benzyloxy)-1H-indazol-3-yl]-N-(3-pyrrolidin-1-ylpropyl)-1H-benzimidazol-6-amine	467.6
660	2-(6-fluoro-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)- 1H-benzimidazol-6-amine	379.5
661	2-(6-chloro-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)-	395.9

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	1H-benzimidazol-6-amine	
662	2-(5-ethoxy-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)-	405.5
	1H-benzimidazol-6-amine	
663	2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-N-(3-pyrrolidin-1-	405.5
	ylpropyl)-1H-benzimidazol-6-amine	
664	2-(7-chloro-1H-indazol-3-yl)-N-(3-pyrrolidin-1-ylpropyl)-	395.9
	1H-benzimidazol-6-amine	
665	N,N-diethyl-N'-[2-(5-fluoro-1H-indazol-3-yl)-1H-	395.5
	benzimidazol-6-yl]-N'-methylpropane-1,3-diamine	
666	N-[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	412.0
	N',N'-diethyl-N-methylpropane-1,3-diamine	
667	N,N-diethyl-N'-methyl-N'-[2-(5-nitro-1H-indazol-3-yl)-	422.5
	1H-benzimidazol-6-yl]propane-1,3-diamine	
668	N-{2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-benzimidazol-6-	483.6
	yl}-N',N'-diethyl-N-methylpropane-1,3-diamine	
669	N,N-diethyl-N'-[2-(6-fluoro-1H-indazol-3-yl)-1H-	395.5
	benzimidazol-6-yl]-N'-methylpropane-1,3-diamine	
670	N-[2-(7-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]-	412.0
	N',N'-diethyl-N-methylpropane-1,3-diamine	

EXAMPLE 671

3-[6-(1,4'-Bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-amine

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To a solution of the product produced in Example 110 (1.0 eq) in ethanol:ethyl acetate (1:1) was added 10% Pd/C (0.5 eq). The reaction vessel was repeatedly purged with nitrogen and then stirred under a hydrogen atmosphere (1 atm) for 48 hours. The product was filtered through Celite with ethanol. The solvent was removed to provide a brown solid which was used without purification. LC/MS (m/z) 416.1 (MH⁺), R_i 1.30 minutes.

EXAMPLES 672-684

Examples 672-684 were synthesized from amino substituted indazole benzimidazoles and isocyanates, using the procedure set forth below for the synthesis of various compounds which include a urea substituent.

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EXAMPLE 672

$N-\{3-[6-(1,4'-Bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl\}-N'-phenylurea$

Benzimidazol-2-yl-1H-indazole-5-ylamine was dissolved in THF and and phenylisocyanate (1.1 equivalents) was added. The mixture was shaken overnight, the solution was concentrated, and the resulting residue was purified by preparatory HPLC. LC/MS (m/z) 535.6 (MH⁺), R₁ 1.93 minutes.

Example	Name	LC/MS (m/z) (MH+)
673	1'-[2-(6-chloro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-5-yl]-1,4'-bipiperidine	437.0
674	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}-N'-isopropylurea	501.6
675	N-benzyl-N'-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}urea	549.7
676	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}-N'-(2,4-dimethoxyphenyl)urea	595.7
677	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}-N'-(tert-butyl)urea	515.7
678	N-[3-(1H-benzimidazol-2-yl)-1H-indazol-5-yl]-N'-(tert-butyl)urea	349.4
679	N-(tert-butyl)-N'-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}urea	447.6
680	N-isopropyl-N'-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}urea	433.5
681	N-(tert-butyl)-N'-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}urea	447.6
682	N-ethyl-N'-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}urea	419.5
683	N-(2-methoxyphenyl)-N'-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}urea	497.6
684	N-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}-N'-[3-(trifluoromethyl)phenyl]urea	535.5

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EXAMPLES 685-689

Examples 685-689 were synthesized from amino substituted indazole-benzimidazoles and acyl halides or sulfonyl halides, using the coupling procedures set forth below for the synthesis of various compounds that include the -N(H)-C(=O)-R or the -N(H)-(SO₂)-R' group.

EXAMPLE 685

 $\label{eq:normalized} $$N-\{3-[6-(1,4'-Bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl\}$ benzamide$

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Benzimidazol-2-yl-1H-indazole-5-ylamine was dissolved in CH₂Cl₂
and benzoyl chloride (1.1 equivalent) was added followed by diisopropylethylamine
(1.1 equivalent). The resulting mixture was allowed to stir overnight. The solution was then concentrated and the resulting residue was purified by preparatory HPLC.
LC/MS (m/z) 520.6 (MH⁺), R₁ 1.86 minutes

EXAMPLE 688

15 N-{3-[6-(1,4'-Bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}methanesulfonamide

3-Benzimidazol-2-yl-1H-indazole-5-ylamine (1 equivalent), methanesulfonyl chloride (1.1 equivalent), and diisopropylethylamine (2 equivalents) in CH₂Cl₂ were stirred for 18 hours. The solvent was evaporated, and the resulting residue was purified by preparatory HPLC. . LC/MS (m/z) 494.6 (MH⁺), R₁ 2.35 minutes.

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Example	Name	LC/MS (m/z) (MH+)
686	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}acetamide	458.6
687	N-{3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-5-yl}-2-furamide	510.6
689	N-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}ethanesulfonamide	440.2

EXAMPLES 690-726

Examples 690-726 were synthesized from amino substituted indazolebenzimidazoles and carbonyl compounds, using the procedure set forth below for 5 Example 710.

EXAMPLE 710

3-(1H-Benzimidazol-2-yl)-N-(1,3-thiazol-2-ylmethyl)-1H-indazol-5-amine

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3-Benzimidazol-2-yl-1H-indazole-5-ylamine (1 equivalent), 2-thiazolecarboxaldehyde(1.1 equivalent), BH₃:pyridine (10 equivalents, 8 M in pyridine) in AcOH:MeOH:CH₂Cl₂ (1:2:2) were stirred for 18 hours at room temperature. The solvent was removed, and the residue was purified by preparatory HPLC. LC/MS (m/z) 347.1 (MH⁺), R_t 1.93 minutes.

Example	Name	LC/MS (m/z) (MH+)
690	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-[(3-methyl-1H-pyrazol-4-yl)methyl]-1H-indazol-5-amine	509.7
691	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(2-furylmethyl)-1H-indazol-5-amine	495.6
692	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(2,3-dihydro-1-benzofuran-5-ylmethyl)-1H-indazol-5-amine	547.7
693	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(1H-imidazol-2-ylmethyl)-1H-indazol-5-amine	495.6
694	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-N-(1,3-thiazol-2-ylmethyl)-1H-indazol-5-amine	512.7

695	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	535.7
	N-(3-methoxybenzyl)-1H-indazol-5-amine	
696	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	498.7
	N-[(2S)-pyrrolidin-2-ylmethyl]-1H-indazol-5-amine	
697	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	552.7
077	N-({5-[(dimethylamino)methyl]-2-furyl}methyl)-1H-	552.7
	indazol-5-amine	
698	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	524.7
090		324.1
	N-[(3,5-dimethylisoxazol-4-yl)methyl]-1H-indazol-5-	
	amine	
699	N-(1H-1,2,3-benzotriazol-5-ylmethyl)-3-[6-(1,4'-	546.7
	bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-	
	5-amine	
700	N-(1H-benzimidazol-5-ylmethyl)-3-[6-(1,4'-	545.7
	bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-	
	5-amine	
701	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	558.1
	N-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)methyl]-	
	1H-indazol-5-amine	
702	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	544.1
102	N-[(4-chloro-1-methyl-1H-pyrazol-3-yl)methyl]-1H-	511.1
	indazol-5-amine	
702		537.7
703	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	337.7
	N-[(2-ethyl-4-methyl-1H-imidazol-5-yl)methyl]-1H-	
	indazol-5-amine	
704	N-(1-(N-hydroxycarbamoyl)(1S,2R)-2-	385.4
	hydroxypropyl){4-[4-(N-	
	ethylcarbamoyl)phenyl]phenyl}carboxamide	
705	N-{4-[(4-fluorobenzyl)oxy]benzyl}-3-[6-(4-	561.7
	methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-	
	indazol-6-amine	
706	N-(1H-benzimidazol-2-ylmethyl)-3-[6-(1,4'-	545.7
	bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-1H-indazol-	
	5-amine	
707	N-benzyl-3-[6-(1,4'-bipiperidin-1'-yl)-1H-	505.7
707	benzimidazol-2-yl]-1H-indazol-5-amine	303.7
	benzinindazor-z-yrj-fff-indazor-3-animie	
708	3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]-	511.7
	N-(cyclohexylmethyl)-1H-indazol-5-amine	
709	N-(1-benzylpiperidin-4-yl)-3-[6-(1,4'-bipiperidin-1'-	588.8
	yl)-1H-benzimidazol-2-yl]-1H-indazol-5-amine	
711	2 (111 homeimidered 2 ml) N ((25) annualidin 2	332.4
711	3-(1H-benzimidazol-2-yl)-N-[(2S)-pyrrolidin-2-	332.4
	ylmethyl]-1H-indazol-5-amine	

712	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N-(1,3-thiazol-2-ylmethyl)-1H-indazol-5-amine	444.6
713	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N-[(2S)-pyrrolidin-2-ylmethyl]-1H-indazol-5-amine	430.6
714	N-(2,5-dimethoxybenzyl)-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-amine	497.6
715	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N-(1,3-thiazol-2-ylmethyl)-1H-indazol-6-amine	444.6
716	N-[(1-methyl-1H-benzimidazol-2-yl)methyl]-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-amine	491.6
717	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N-[(2-phenyl-1H-imidazol-4-yl)methyl]-1H-indazol-6-amine	503.6
718	N-benzyl-3-[6-(4-methylpiperazin-1-yl)-1H- benzimidazol-2-yl]-1H-indazol-6-amine	437.5
719	N-[(2-ethyl-4-methyl-1H-imidazol-5-yl)methyl]-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-amine	469.6
720	N-(2-furylmethyl)-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-amine	427.5
721	N-[(4-methoxyquinolin-2-yl)methyl]-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-amine	518.6
722	3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-N-(1-methylpiperidin-4-yl)-1H-indazol-6-amine	444.6
723	N-(2-fluoro-5-methoxybenzyl)-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-amine	485.6
724	N-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}-2-furamide	441.5
725	N-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}-1,3-oxazole-5-carboxamide	442.5
726	N-{3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl}acetamide	389.5

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EXAMPLE 727

Synthesis of [(1Z)-2-aza-1-(4-methylpiperazinyl)-2-phenylvinyl]{3-[6-(4-piperidylpiperidyl)benzimidazol-2-yl](1H-indazol-5-yl)}amine

3-[6-(4-piperidylpiperidyl)benzimidazol-2-yl]-1H-indazole-5-ylamine
was dissolved in THF and shaken with benzenisothiocyanate (1.1 equivalents) for 18 hours. EDC-HCl (1.1 equivalents) and N-methylpiperazine (3 equivalents) were then added. The resulting solution was shaken for 18 hours. The solvent was then evaporated, and the residue was purified by preparatory HPLC to give [(1Z)-2-aza-1-(4-methyl-piperazinyl)-2-phenylvinyl]{3-[6-(4-piperidylpiperidyl)benzimidazol-2-yl](1H-indazol-5-yl)}amine. LC/MS (m/z) 617.5 (MH+), R₁ 2.65 minutes.

EXAMPLE 728

N'-[3-(1H-Benzoimidazol-2-yl)-1H-indazol-5-yl]-N,N-dimethyl-propane-1,3-diamine

Synthesis of 5-Bromo-1-(2-trimethylsilanyl-ethoxymethyl)-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-yl]-1H-indazole

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A reaction mixture of 3-benzimidazol-2-yl-5-bromo-1H-indazole in CH₂Cl₂ and aqueous 50% NaOH solution was cooled to 0°C and charged with SEMCl (2.2 equivalents). The reaction was stirred overnight and the cooling bath was gradually allowed to warm to room temperature. The reaction was partitioned between water and methylene chloride and the layers separated. The aqueous phase was extracted with CH₂Cl₂ (3X) and the organic extracts were combined and washed with brine. The resulting crude residue was purified by flash chromatography to give 5-bromo-1-(2-trimethylsilanyl-ethoxymethyl)-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-yl]-1H-indazole. LC/MS (m/z) 573.1 (MH+), R₁ 4.29 minutes.

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Synthesis of N,N-Dimethyl-N'- $\{1-(2-trimethylsilanyl-ethoxymethyl)-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-propane-1,3-diamine$

To a solution of 5-bromo-1-(2-trimethylsilanyl-ethoxymethyl)-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-yl]-1H-indazole in dry toluene was added Pd₂(dba)₃ (0.02 equivalents), (R)-BINAP (0.06 equivalents), N,N dimethyl propyldiamine (1.6 equivalents), and sodium t-butoxide (1.2 equivalents). The resulting reaction mixture was subjected to microwave irradiation (≈ 300 watts, 120°C, 10 minutes). The crude reaction product was purified by chromatography to furnish N,N-Dimethyl-N'-{1-(2-trimethylsilanyl-ethoxymethyl)-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-propane-1,3-diamine. LC/MS (m/z) 595.3 (MH+), R₁ 2.95 minutes.

 $Synthesis\ of\ N'-[3-(1H-Benzoimidazol-2-yl)-1H-indazol-5-yl]-N, N-dimethyl-propane-1, 3-diamine$

- 15 A solution of N,N-dimethyl-N'-{1-(2-trimethylsilanyl-ethoxymethyl)-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-propane-1,3-diamine in THF was treated with ethylene diamine (20 equivalents) and tetrabutylammonium fluoride (20 equivalents) and heated at 70°C overnight. The resulting crude residue was purified by reverse phase HPLC to N'-[3-(1H-
- 20 Benzoimidazol-2-yl)-1H-indazol-5-yl]-N,N-dimethyl-propane-1,3-diamine. LC/MS (m/z) 335.1 (MH+), R₁ 1.30 minutes.

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EXAMPLE 729

2-{4-[2-(5-Ethoxy-1H-indazol-3-yl)-3H-benzimidazol-5-yl]-piperazin-1-yl}-ethanol

Synthesis of 5-Ethoxyindole

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5-Hydroxyindole (1.0 equivalents) was dissolved in dry, degassed acetone. EtBr (5.0 equivalents) and CS₂CO₃ (2.5 equivalents) were added, and the resulting solution was stirred for 18 hours. The reaction mixture was filtered through a Celite plug. The solvent was evaporated and the product purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the desired indole ether title compound. LC/MS (m/z) 162.1 (MH+), R₁ 2.45 minutes.

Synthesis of 5-Ethoxy-1H-indazole-3-carbaldehyde

The formation of 5-ethoxy-1H-indazole-3-carbaldehyde from 5ethoxyindole was carried out using the procedures described above in Example 4. LC/MS (m/z) 191.1 (MH⁺), R_t 2.14 minutes.

Synthesis of 2-{4-[2-(5-Ethoxy-1H-indazol-3-yl)-3H-benzimidazol-5-yl]-piperazin-1-yl}-ethanol

The formation of 2-{4-[2-(5-ethoxy-1H-indazol-3-yl)-3H-20 benzimidazol-5-yl]-piperazin-1-yl}-ethanol was carried out using 5-ethoxy-1Hindazole-3-carbaldehyde and 2-[4-(3,4-diaminophenyl)-piperazin-1-yl]-ethanol using

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the method described above in Example 4. LC/MS (m/z) 407.3, (MH+), R_t 2.65 minutes.

EXAMPLE 730

3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-(5-nitro-pyridin-2-yloxy)-1H-indazole

Synthesis of 5-(5-Nitro-pyridin-2-yloxy)-1H-indole

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NaH (1.1 equivalents) was added to a solution of 5-hydroxyindole (1.0 equivalent) in NMP. The resulting mixture stirred for 2 hours at room temperature. 2-Chloro-5-nitropyridine (1.1 equivalents) was added and the solution was heated to 100°C for 2 hours. The solution was cooled and poured into water. The aqueous layer was extracted with EtOAc three times. The organic layers were then combined and concentrated to yield the desired indole heteroaryl ether 5-(5-nitro-pyridin-2-yloxy)-1H-indole.

15 Synthesis of 5-(5-Nitro-pyridin-2-yloxy)-1H-indazole-3-carbaldehyde

The formation of 5-(5-nitro-pyridin-2-yloxy)-1H-indazole-3-carbaldehyde from 5-(5-nitro-pyridin-2-yloxy)-1H-indole was carried using the method described above in Example 4. LC/MS (m/z) 285.2 (MH+), R₁ 2.43 minutes.

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Synthesis of 3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-(5-nitro-pyridin-2-yloxy)-1H-indazole-

The title compound was synthesized from 5-(5-nitro-pyridin-2-yloxy)-1H-indazole-3-carbaldehyde and 4-(4-methyl-piperazin-1-yl)-benzene-1,2-diamine using the method described above in Example 4. LC/MS (m/z) 471.3 (MH+), R₁ 2.94 minutes.

EXAMPLE 731

3-(1H-Benzoimidazol-2-yl)-1H-indazol-5-ol

desired 5-hydroxyindole benzimidazole.

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A solution of 5-hydroxyindole (1.0 equivalent), benzyl chloroformate

(1.1 equivalents), and diisopropylethylamine (2.0 equivalents) in CH₂Cl₂ was stirred for 18 hours. The solution is concentrated to yield the desired CBz protected indole ether. The product is then reacted with NaNO₂ in HCl and dioxane as previously described, followed by reaction with phenylenediamine in EtOH and toluene using the methods described above to yield the Cbz protected indazole benzimidazole.

The Cbz-protected product is deprotected using 10% Pd/C and H₂ to provide the

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EXAMPLE 732

4-[2-(5-Fluoro-1H-indazol-3-yl)-1-methyl-1H-benzoimidazol-5-yloxy]-pyridine-2-carboxylic acid methylamide

Synthesis of 4-(4-Amino-3-nitro-phenoxy)-pyridine-2-carboxylic acid methylamide

A mixture containing 4-amino-3-nitrophenol (1 equivalent) and potassium bis(trimethylsilyl)amide (2 equivalents) was stirred in dimethylformamide for 2 hours at room temperature. [4-chloro-(2-pyridiyl)]-N-methylcarboxamide (1 equivalent) and potassium carbonate (1.5 equivalents) were added to the mixture, and the reaction was stirred at 90°C for 3 days. The reaction mixture was then concentrated and partitioned between ethyl acetate and water. The organic layer was separated, washed with brine (2x), dried, filtered, and concentrated to give brown solid. LC/MS (m/z) 289.2 (MH+), R₁ 2.18 minutes.

15 Synthesis of 4-(4-Methylamino-3-nitro-phenoxy)-pyridine-2-carboxylic acid methylamide

A solution of 4-(4-amino-3-nitro-phenoxy)-pyridine-2-carboxylic acid methylamide (1 equivalent) in CH₂Cl₂ was treated with trifluoroacetic anhydride (1 equivalent) and stirred for 10 minutes at 0°C. The mixture was quenched with a saturated NaHCO₃ solution. The organic layer was separated and washed with water and brine, dried, and evaporated to yield the trifluoroacetamide.

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To the solution of the trifluoroacetamide (1 equivalent) in a mixture of toluene:acetonitrile (approximately 4:1) and sodium hydroxide solution (50%) was added benzyltrimethylammonium chloride (1 equivalent) and dimethyl sulfate (1.5 equivalents). The biphasic mixture was stirred overnight at room temperature. The mixture was evaporated and then taken up in ethyl acetate, washed with water (2x) and brine (2x), dried, and evaporated to yield the title compound as a reddish orange solid. LC/MS (m/z) 303.3 (MH+), R₁ 2.42 minutes.

Synthesis of 4-(3-Amino-4-methylamino-phenoxy)-pyridine-2-carboxylic acid methylamide

$$\begin{array}{c} O_2N \\ N \\ N \\ N \end{array} \begin{array}{c} Pd/C, H_2, EtOH \\ N \\ N \\ N \end{array} \begin{array}{c} O_2N \\ N \\ N \\ N \end{array}$$

4-(4-Methylamino-3-nitro-phenoxy)-pyridine-2-carboxylic acid methylamide was reduced using the hydrogenation procedure described in Method 1. LC/MS (m/z) 273.3 (MH⁺), R₁ 1.63 minutes.

Synthesis of 4-[2-(5-Fluoro-1H-indazol-3-yl)-1-methyl-1H-benzoimidazol-5-yloxy]-pyridine-2-carboxylic acid methylamide

The title compound was synthesized from 5-fluoro-1H-indazole-3-carbaldehyde and 4-(3-amino-4-methylamino-phenoxy)-pyridine-2-carboxylic acid

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methylamide as described above in Example 4. LC/MS (m/z) 417.4 (MH+), R₁ 3.62 minutes.

EXAMPLE 733

4-[2-(5-Fluoro-1H-indazol-3-yl)-1H-benzoimidazol-5-yloxy]-pyridine-2-carboxylic acid methylamide

Synthesis of 4-(3,4-Diamino-phenoxy)-pyridine-2-carboxylic acid methylamide

4-(4-Amino-3-nitro-phenoxy)-pyridine-2-carboxylic acid methylamide was reduced using the hydrogenation procedure described in Method 1. LC/MS (m/z) 259.2 (MH+), R₁ 1.32 minutes.

Synthesis of 4-[2-(5-Fluoro-1H-indazol-3-yl)-1H-benzoimidazol-5-yloxy]-pyridine-2-carboxylic acid methylamide

The title compound was synthesized from 5-fluoro-1H-indazole-3-carbaldehyde and 4-(3,4-diamino-phenoxy)-pyridine-2-carboxylic acid methylamide using the method described above in Example 4. LC/MS (m/z) 403.1 (MH+), R₁ 2.26 minutes.

EXAMPLES 734-741

Example	Name
l .	{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine

735	{4-[2-(5-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
736	{4-[2-(5-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
737	dimethyl-(5-methyl-4-{2-[5-(1-methyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
738	1'-[2-(5-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
739	1'-[2-(5-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
740	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-(1-methyl-piperidin-3-yloxy)-1H-indazole
741	1'-{2-[5-(1-methyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl

EXAMPLE 742

1'-[2-(4-Ethoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

Synthesis of 4-Ethoxy-1H-indole

4-Hydroxyindole (1.0 equivalents) is dissolved in dry, degassed acetone. EtBr (5.0 equivalents) and Cs₂CO₃ (2.5 equivalents) are added, and the resulting solution is stirred for 18 hours. The reaction mixture is filtered through a Celite plug. The solvent is evaporated, and the product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the title compound.

10 Synthesis of 4-Ethoxy-1H-indazole-3-carbaldehyde

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The formation of the title compound from 4-ethoxy-1H-indole is carried out using the procedure described above in Example 4.

Synthesis of 1'-[2-(4-Ethoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

The formation of the title compound is carried out using 4-ethoxy-1H-indazole-3-carbaldehyde and 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine using the method described above in Example 4.

EXAMPLES 743-754

Example	Name
743	{4-[2-(4-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
744	{4-[2-(4-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
745	{4-[2-(4-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
746	(4-{2-[4-(1-ethyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-amine
747	4-methoxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
748	4-isopropoxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
749	4-benzyloxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
750	4-(1-ethyl-piperidin-3-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
751	1'-[2-(4-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
752	1'-[2-(4-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
753	1'-[2-(4-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
754	1'-{2-[4-(1-ethyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-

benzoimidazol-5-yl}-[1,4']bipiperidinyl

EXAMPLE 755

1'-[2-(6-Ethoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

Synthesis of 6-Ethoxy-1H-indole

6-Hydroxyindole (1.0 equivalents) is dissolved in dry, degassed acetone. EtBr (5.0 equivalents) and Cs₂CO₃ (2.5 equivalents) are added, and the resulting solution is stirred for 18 hours. The reaction mixture is filtered through a Celite plug. The solvent is evaporated, and the product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the title compound.

10 Synthesis of 6-Ethoxy-1H-indazole-3-carbaldehyde

The formation of the title compound from 6-ethoxy-1H-indole is carried out using the procedure described above in Example 4.

Synthesis of 1'-[2-(6-Ethoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-

15 [1,4']bipiperidinyl

The formation of the title compound is carried out using 6-ethoxy-1H-indazole-3-carbaldehyde and 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine using the method described above in Example 4.

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EXAMPLES 756-767

Example	Name
756	{4-[2-(6-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
757	{4-[2-(6-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
758	{4-[2-(6-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
759	(4-{2-[6-(1-ethyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethylamine
760	6-methoxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
761	6-isopropoxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
762	6-benzyloxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
763	6-(1-ethyl-piperidin-3-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
764	1'-[2-(6-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
765	1'-[2-(6-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
766	1'-[2-(6-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl
767	1'-{2-[6-(1-ethyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl

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EXAMPLE 768

1'-[2-(7-Ethoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-Synthesis of 7-Ethoxy-1H-indole

7-Hydroxyindole (1.0 equivalents) is dissolved in dry, degassed acetone. EtBr (5.0 equivalents) and Cs₂CO₃ (2.5 equivalents) are added, and the resulting solution is stirred for 18 hours. The reaction mixture is filtered through a Celite plug. The solvent is evaporated, and the product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the title compound.

10 Synthesis of 7-Ethoxy-1H-indazole-3-carbaldehyde

The formation of the title compound from 7-ethoxy-1H-indole is carried out using the procedure described above in Example 4.

Synthesis of 1'-[2-(7-Ethoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]15 [1,4']bipiperidinyl

The formation of the title compound is carried out using 7-ethoxy-1H-indazole-3-carbaldehyde and 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine using the method described above in Example 4.

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EXAMPLES 769-780

The compounds in the following table are synthesized using the procedures described above.

Example	Name
769	[4-[2-(7-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-
	methyl-morpholin-2-ylmethyl}-dimethyl-amine
770	{4-[2-(7-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-
	methyl-morpholin-2-ylmethyl}-dimethyl-amine
771	{4-[2-(7-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-
	methyl-morpholin-2-ylmethyl}-dimethyl-amine
772	(4-{2-[7-(1-ethyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-
	benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-
	amine
773	7-methoxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-
	1H-indazole
774	7-isopropoxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-
	yl]-1H-indazole
775	7-benzyloxy-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-
	yl]-1H-indazole
776	7-(1-ethyl-piperidin-3-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-
	benzoimidazol-2-yl]-1H-indazole
777	1'-[2-(7-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4']bipiperidinyl
778	1'-[2-(7-isopropoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4']bipiperidinyl
779	1'-[2-(7-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4']bipiperidinyl
780	1'-{2-[7-(1-ethyl-piperidin-3-yloxy)-1H-indazol-3-yl]-3H-
	benzoimidazol-5-yl}-[1,4']bipiperidinyl

EXAMPLES 781-792

The compounds in the following table are synthesized using the procedures described in Example 730.

5

Example	Name
781	dimethyl-(5-methyl-4-{2-[5-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
782	(4-{2-[5-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-

	amine
783	2-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yloxy}-nicotinonitrile
784	dimethyl-(5-methyl-4-{2-[5-(4-methyl-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
785	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-(pyridin-2-yloxy)-1H-indazole
786	5-(3-methoxy-pyridin-2-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
787	2-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yloxy}-nicotinonitrile
788	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-(4-methyl-pyridin-2-yloxy)-1H-indazole
789	1'-{2-[5-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl
790	1'-{2-[5-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl
791	2-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-5-yloxy]-nicotinonitrile
792	1'-{2-[5-(4-methyl-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl

EXAMPLE 793

 $\label{lem:conditional} 3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-4-(5-nitro-pyridin-2-yloxy)-1H-indazole$

Synthesis of 4-(5-Nitropyridin-2-yloxy)-1H-indole

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NaH (1.1 equivalents) is added to a solution of 4-hydroxyindole (1.0 equivalent) in NMP. The resulting mixture is stirred for 2 hours at room temperature. 2-Chloro-5-nitropyridine (1.1 equivalents) is added and the solution is

heated to 100°C for 2 hours. The solution is cooled and poured into water. The aqueous layer is extracted with EtOAc three times. The organic layers are combined and concentrated to yield the title compound.

Synthesis of 4-(5-Nitro-pyridin-2-yloxy)-1H-indazole-3-carbaldehyde

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The formation of the title compound from 4-(5-nitropyridin-2-yloxy)-1H-indole is carried out using the procedure described above in Example 4.

Synthesis of 3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-4-(5-nitro-pyridin-2-yloxy)-1H-indazole

The formation of the title compound is carried out using 4-(5-nitropyridin-2-yloxy)-1H-indazole-3-carbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine using the method described above in Example 4.

EXAMPLES 794-805

Example	Name
794	dimethyl-(5-methyl-4-{2-[4-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
795	(4-{2-[4-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-amine
796	2-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yloxy}-nicotinonitrile
797	dimethyl-(5-methyl-4-{2-[4-(4-methyl-pyridin-2-yloxy)-1H-indazol-

	3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
798	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-4-(pyridin-2-yloxy)-1H-indazole
799	4-(3-methoxy-pyridin-2-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
800	2-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yloxy}-nicotinonitrile
801	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-4-(4-methyl-pyridin-2-yloxy)-1H-indazole
802	1'-{2-[4-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl
803	1'-{2-[4-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl
804	2-[3-(6-[1,4']Bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yloxy]-nicotinonitrile
805	1'-{2-[4-(4-Methyl-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl

EXAMPLE 806

3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-6-(5-nitro-pyridin-2-yloxy)-1H-indazole

Synthesis of 6-(5-Nitropyridin-2-yloxy)-1H-indole

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NaH (1.1 equivalents) is added to a solution of 6-hydroxyindole (1.0 equivalent) in NMP. The resulting mixture is stirred for 2 hours at room temperature. 2-Chloro-5-nitropyridine (1.1 equivalents) is added and the solution is heated to 100°C for 2 hours. The solution is cooled and poured into water. The aqueous layer is extracted with EtOAc three times. The organic layers are combined and concentrated to yield the titled compound.

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Synthesis of 6-(5-Nitropyridin-2-yloxy)-1H-indazole-3-carbaldehyde

The formation of the title compound from 6-(5-nitropyridin-2-yloxy)-1H-indole is carried out using the procedure described in Example 4.

5 Synthesis of 3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-6-(5-nitro-pyridin-2-yloxy)-1H-indazole

The formation of the title compound is carried out using 6-(5-nitropyridin-2-yloxy)-1H-indazole-3-carbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine using the method described above in Example 4.

EXAMPLES 807-818

The compounds in the following table are synthesized using the procedures described above.

Example	Name
807	Dimethyl-(5-methyl-4-{2-[6-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
808	(4-{2-[6-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethylamine
809	2-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yloxy}-nicotinonitrile
810	Dimethyl-(5-methyl-4-{2-[6-(4-methyl-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
811	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-6-(pyridin-2-yloxy)-1H-indazole
812	6-(3-methoxy-pyridin-2-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
813	2-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yloxy}-nicotinonitrile
814	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-6-(4-methyl-pyridin-2-yloxy)-1H-indazole

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815	1'-{2-[6-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl
816	1'-{2-[6-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl
817	2-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yloxy]-nicotinonitrile
818	1'-{2-[6-(4-methyl-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-[1,4']bipiperidinyl

EXAMPLE 819

 $\label{eq:continuous} 3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-7-(5-nitro-pyridin-2-yloxy)-1H-indazole$

5 Synthesis of 7-(5-Nitropyridin-2-yloxy)-1H-indole

NaH (1.1 equivalents) is added to a solution of 7-hydroxyindole (1.0 equivalent) in NMP. The resulting mixture is stirred for 2 hours at room temperature. 2-Chloro-5-nitropyridine (1.1 equivalents) is added and the solution is heated to 100°C for 2 hours. The solution is cooled and poured into water. The aqueous layer is extracted with EtOAc three times. The organic layers are combined and concentrated to yield the desired indole heteroaryl ether.

Synthesis of 7-(5-Nitropyridin-2-yloxy)-1H-indazole-3-carbaldehyde

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The formation of the title compound from 7-(5-nitropyridin-2-yloxy)-1H-indole is carried out using the procedure described above in Example 4.

Synthesis of 3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-7-(5-nitropyridin-2-yloxy)-1H-indazole

5 The formation of the title compound is carried out using 7-(5-nitropyridin-2-yloxy)-1H-indazole-3-carbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine using the method described above in Example 4.

EXAMPLES 820-831

The compounds in the following table are synthesized using the procedures described above.

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Example	Name
820	dimethyl-(5-methyl-4-{2-[7-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-
	benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
821	(4-{2-[7-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-
	benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-amine
822	2-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazol-7-yloxy}-nicotinonitrile
823	dimethyl-(5-methyl-4-{2-[7-(4-methyl-pyridin-2-yloxy)-1H-indazol-
	3-yl]-3H-benzoimidazol-5-yl}-morpholin-2-ylmethyl)-amine
824	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-7-(pyridin-2-
	yloxy)-1H-indazole
825	7-(3-methoxy-pyridin-2-yloxy)-3-[6-(4-methyl-piperazin-1-yl)-1H-
	benzoimidazol-2-yl]-1H-indazole
826	2-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-
	indazol-7-yloxy}-nicotinonitrile
827	3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-7-(4-methyl-
	pyridin-2-yloxy)-1H-indazole
828	1'-{2-[7-(pyridin-2-yloxy)-1H-indazol-3-yl]-3H-benzoimidazol-5-
	yl}-[1,4']bipiperidinyl
829	1'-{2-[7-(3-methoxy-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-
	benzoimidazol-5-yl}-[1,4']bipiperidinyl
830	2-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-
	indazol-7-yloxy]-nicotinonitrile
831	1'-{2-[7-(4-methyl-pyridin-2-yloxy)-1H-indazol-3-yl]-3H-

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	benzoimidazol-5-yl}-[1,4']bipiperidinyl
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EXAMPLES 832-842

The compounds in the following table are synthesized using the procedures described in Example 685.

Example	Name
832	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazol-5-yl}-acetamide
833	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazol-5-yl}-2,2-dimethyl-propionamide
834	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazol-5-yl}-2,4-difluoro-benzamide
835	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazol-5-yl}-2-methoxy-benzamide
836	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-
	indazol-5-yl}-acetamide
837	2,2-dimethyl-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-
	2-yl]-1H-indazol-5-yl}-propionamide
838	2,4-difluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-
	2-yl]-1H-indazol-5-yl}-benzamide
839	2-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-
	yl]-1H-indazol-5-yl}-benzamide
840	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-
	indazol-5-yl]-2,2-dimethyl-propionamide
841	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-
	indazol-5-yl]-2,4-difluoro-benzamide
842	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-
	indazol-5-yl]-2-methoxy-benzamide

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EXAMPLES 843-854

Example	Name
843	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazol-5-yl}-C,C,C-trifluoro-
	methanesulfonamide

844	thiophene-2-sulfonic acid {3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-amide
845	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-benzenesulfonamide
846	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-4-methoxy-benzenesulfonamide
847	C,C,C-trifluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-methanesulfonamide
848	thiophene-2-sulfonic acid {3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-amide
849	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-benzenesulfonamide
850	4-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-benzenesulfonamide
· 851	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-5-yl]-C,C,C-trifluoro-methanesulfonamide
852	thiophene-2-sulfonic acid [3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-5-yl]-amide
853	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-5-yl]-benzenesulfonamide
854	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-5-yl]-4-methoxy-benzenesulfonamide

EXAMPLES 855-865

The compounds in the following table are synthesized using the procedures described in Example 685 using 3-benzimidazol-2-yl-1H-indazol-6-

5 ylamine as the starting material.

Example	Name
855	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-acetamide
856	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-2,2-dimethyl-propionamide
857	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-2,4-difluoro-benzamide
858	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-2-methoxy-benzamide
859	2,2-dimethyl-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-propionamide

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860	2,4-difluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-benzamide
861	2-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-benzamide
862	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-acetamide
863	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-2,2-dimethyl-propionamide
864	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-2,4-difluoro-benzamide
865	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-2-methoxy-benzamide

EXAMPLES 866-877

The compounds in the following table are synthesized using the procedures described in Example 688 using 3-benzimidazol-2-yl-1H-indazol-6-ylamine as the starting material.

5

Example	Name
866	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-C,C,C-trifluoromethanesulfonamide
867	thiophene-2-sulfonic acid {3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-amide
868	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-benzenesulfonamide
869	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-4-methoxy-benzenesulfonamide
870	C,C,C-trifluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-methanesulfonamide
871	thiophene-2-sulfonic acid {3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-amide
872	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-benzenesulfonamide
873	4-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-yl}-benzenesulfonamide
874	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-C,C,C-trifluoro-methanesulfonamide
875	Thiophene-2-sulfonic acid [3-(6-[1,4']bipiperidinyl-1'-yl-1H-

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	benzoimidazol-2-yl)-1H-indazol-6-yl]-amide
876	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-benzenesulfonamide
877	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-6-yl]-4-methoxy-benzenesulfonamide

EXAMPLE 878

$N-\{3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl\}-benzamide$

3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-ylamine is dissolved in CH₂Cl₂ and benzoyl chloride (1.1 equivalent) is added followed by diisopropylethylamine (1.1 equivalent). The resulting mixture is stirred overnight. The solution is then concentrated and the resulting residue is purified by preparatory HPLC to provide the title compound.

EXAMPLES 879-890

The compounds in the following table are synthesized using the procedures described above.

10

Example	Name
879	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-acetamide
880	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-2,2-dimethyl-propionamide
881	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-2,4-difluoro-benzamide
882	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-2-methoxy-benzamide
883	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-acetamide
884	2,2-dimethyl-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-propionamide
885	2,4-difluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-benzamide

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886	2-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-benzamide
887	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-acetamide
888	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-2,2-dimethyl-propionamide
889	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-2,4-difluoro-benzamide
890	N-[3-(6-[1,4']Bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-2-methoxy-benzamide

EXAMPLE 891

$N-\{3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl\}-methanesulfonamide$

3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-ylamine (1 equivalent), methanesulfonyl chloride (1.1 equivalent), and diisopropylethylamine (2 equivalents) in CH₂Cl₂ are stirred for 18 hours. The solvent is evaporated, and the resulting residue is purified by preparatory HPLC to provide the title compound.

EXAMPLES 892-903

Example	Name
892	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-C,C,C-trifluoro-methanesulfonamide
893	thiophene-2-sulfonic acid {3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-amide
894	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-benzenesulfonamide
895	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-4-methoxy-benzenesulfonamide

896	C,C,C-trifluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-methanesulfonamide
897	thiophene-2-sulfonic acid {3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-amide
898	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-benzenesulfonamide
899	4-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-yl}-benzenesulfonamide
900	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-C,C,C-trifluoro-methanesulfonamide
901	thiophene-2-sulfonic acid [3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-amide
902	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-benzenesulfonamide
903	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-4-methoxy-benzenesulfonamide

EXAMPLE 904

3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-7-nitro-1H-indazole

Synthesis of 7-Nitro-1H-indazole-3-carbaldehyde

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The formation of 7-nitro-1H-indazole-3-carbaldehyde is carried out from the commercially available 7-nitroindole using the method described above in Example 4.

Synthesis of 3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-7-nitro-1H-10 indazole

The formation of the title compound from 7-nitro-1H-indazole-3-carbaldehyde and 4-(4-methylpiperazin-1-yl)benzene-1,2-diamine is carried out using the procedure described above in Example 4.

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EXAMPLE 905

3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ylamine

The title compound is obtained by reducing the nitro group of 3-[6-(4-methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-7-nitro-1H-indazole of Example 742 using the method described in Method 1.

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EXAMPLE 906

N-{3-[6-(4-Methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-benzamide

The 3-[6-(4-methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ylamine of Example 743 is dissolved in CH₂Cl₂ and benzoyl chloride (1.1 equivalent) is added followed by diisopropylethylamine (1.1 equivalent). The resulting mixture is stirred overnight. The solution is then concentrated and the resulting residue is purified by preparatory HPLC to provide the title compound.

EXAMPLES 907-918

Example	Name
907	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-acetamide
908	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-2,2-dimethyl-propionamide
909	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-2,4-difluoro-benzamide
910	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-2-methoxy-benzamide
911	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-acetamide
912	2,2-dimethyl-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-propionamide

913	2,4-difluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-benzamide
914	2-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-benzamide
915	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-acetamide
916	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-2,2-dimethyl-propionamide
917	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-2,4-difluoro-benzamide
918	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-2-methoxy-benzamide

EXAMPLE 919

$N-\{3-[6-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl\}-methanesulfonamide$

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3-[6-(4-methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ylamine (1 equivalent), methanesulfonyl chloride (1.1 equivalent), and diisopropylethylamine (2 equivalents) in CH₂Cl₂ are stirred for 18 hours. The solvent is evaporated, and the resulting residue is purified by preparatory HPLC to provide the title compound.

EXAMPLES 920-931

Example	Name
920	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-C,C,C-trifluoromethanesulfonamide
921	thiophene-2-sulfonic acid {3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-amide
922	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-benzenesulfonamide
923	N-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-4-methoxy-

	benzenesulfonamide
924	C,C,C-trifluoro-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-methanesulfonamide
925	thiophene-2-sulfonic acid {3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-amide
926	N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-benzenesulfonamide
927	4-methoxy-N-{3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-yl}-benzenesulfonamide
928	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-C,C,C-trifluoro-methanesulfonamide
929	thiophene-2-sulfonic acid [3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-amide
930	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-benzenesulfonamide
931	N-[3-(6-[1,4']bipiperidinyl-1'-yl-1H-benzoimidazol-2-yl)-1H-indazol-7-yl]-4-methoxy-benzenesulfonamide

EXAMPLE 932

 $\label{eq:condition} (\{(2R,5S)-4-[2-(6-Fluoro(1H-indazol-3-yl))benzimidazol-6-yl]-5-methylmorpholin-2-yl\} methyl) diethylamine$

5 Synthesis of {[(2R,5S)-5-Methyl-4-benzylmorpholin-2-yl]methyl}diethylamine

The title compound is obtained from (2S,5S)-2-(chloromethyl)-5-methyl-4-benzylmorpholine (see Method 8 Steps 1 and 2) displacing the chloride with diethylamine under the same reaction conditions used in Method 8 Step 3.

10 Synthesis of [((2S,5S)-5-Methylmorpholin-2-yl)methyl]diethylamine

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The formation of the title compound is carried out using the same procedure described in Method 8 Step 4 from {[(5S,2R)-5-methyl-4-benzylmorpholin-2-yl]methyl}diethylamine.

5 Synthesis of {[(2R,5S)-4-(3-Amino-4-nitrophenyl)-5-methylmorpholin-2yl]methyl}diethylamine

HN O Et
$$H_2N$$
 F Et_3N , NMP O_2N O_2

The formation of the title compound is carried out using the same procedure described in Method 8 Step 5 using [((2S,5S)-5-methylmorpholin-2-yl)methyl]diethylamine and 5-fluoro-2-nitro-phenylamine.

Synthesis of {[(2R,5S)-4-(3,4-Diaminophenyl)-5-methylmorpholin-2-yl]methyl}diethylamine

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$$H_2N$$
 H_2N
 H_2
 $H_$

The formation of the title compound is carried out using the same procedure described in Method 8 Step 6 {[(2R,5S)-4-(3-amino-4-nitrophenyl)-5-methylmorpholin-2yl]methyl}diethylamine.

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Synthesis of $({(2R,5S)-4-[2-(6-Fluoro(1H-indazol-3-yl))benzimidazol-6-yl]-5-methylmorpholin-2-yl}methyl)diethylamine$

The title compund is synthesized according to the general procedure described in Example 4 with {[(2R,5S)-4-(3,4-diaminophenyl)-5-methylmorpholin-2-yl]methyl}diethylamine and 6-fluoro-1H-indazole-3-carbaldehyde.

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EXAMPLES 933-940

The compounds in the following table are synthesized using the procedures described above in Example 932.

Example	Name
933	(2R,5S)-diethyl-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
934	(2R,5S)-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
,	5-methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
935	(2R,5S)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-diethyl-amine
936	(2R,5S)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
937	(2R,5S)-diethyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
938	(2R,5S)-isopropyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-methyl-amine
939	(2R,5S)-3-[6-(2-azetidin-1-ylmethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-6-fluoro-1H-indazole
940	(2R,5S)-6-fluoro-3-[6-(5-methyl-2-pyrrolidin-1-ylmethyl-morpholin-
	4-yl)-1H-benzoimidazol-2-yl]-1H-indazole

EXAMPLES 941-964

The compounds in the following table are synthesized using the procedures described above in Example 932 starting from the appropriate (2S,5R)-2-(chloromethyl)-5-methyl-4-benzylmorpholine, (2R,5S)-2-(chloromethyl)-5-methyl-4-benzylmorpholine.

Example	Name
941	(2S,5S)-diethyl-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-
	5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
942	(2S,5S)-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-
	methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
943	(2S,5S)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-
	methyl-morpholin-2-ylmethyl}-diethyl-amine
944	(2S,5S)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-
	methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
945	$(2S,5S)$ -diethyl- $\{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-indazol-3-yl)-3H-indazol-3-yl\}$
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
946	(2S,5S)-isopropyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-methyl-amine
947	(2S,5S)-3-[6-(2-azetidin-1-ylmethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-6-fluoro-1H-indazole
948	(2S,5S)-6-fluoro-3-[6-(5-methyl-2-pyrrolidin-1-ylmethyl-morpholin-
	4-yl)-1H-benzoimidazol-2-yl]-1H-indazole
949	(2S,5R)-diethyl-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
950	(2S,5R)-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
951	(2S,5R)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-diethyl-amine
952	(2S,5R)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
953	$(2S,5R)$ -diethyl- $\{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-indazol-3-yl)-3H-indazol-3-yl\}$
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
954	(2S,5R)-isopropyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-methyl-amine
955	(2S,5R)-3-[6-(2-azetidin-1-ylmethyl-5-methyl-morpholin-4-yl)-1H-
	benzoimidazol-2-yl]-6-fluoro-1H-indazole
956	(2S,5R)-6-fluoro-3-[6-(5-methyl-2-pyrrolidin-1-ylmethyl-morpholin-
	4-yl)-1H-benzoimidazol-2-yl]-1H-indazole
957	(2R,5R)-diethyl-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
958	(2R,5R)-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
959	(2R,5R)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-diethyl-amine
960	(2R,5R)-{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	5-methyl-morpholin-2-ylmethyl}-isopropyl-methyl-amine
961	(2R,5R)-diethyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-

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	benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-amine
962	(2R,5R)-isopropyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-methyl-amine
963	(2R,5R)-3-[6-(2-azetidin-1-ylmethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-6-fluoro-1H-indazole
964	(2R,5R)-6-fluoro-3-[6-(5-methyl-2-pyrrolidin-1-ylmethyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazole

EXAMPLES 965-972

The compounds in the following table are synthesized using the procedures described above in Example 932 using (S)-(+)-2-amino-1-butanol or (R)-(-)-2-amino-1-butanol and performing the displacement on the chloromethyl intermediate with dimethylamine or diethylamine.

Example	Name
965	(2R,5S)-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-dimethyl-amine
966	(2R,5S)-diethyl-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-amine
967	(2R,5R)-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-dimethyl-amine
968	(2R-5R)-diethyl-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-amine
969	(2S,5S)-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-
	5-yl]-morpholin-2-ylmethyl}-dimethyl-amine
970	(2S-5S)-diethyl-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-amine
971	(2S,5R)-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-dimethyl-amine
972	(2S-5R)-diethyl-{5-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-
}	benzoimidazol-5-yl]-morpholin-2-ylmethyl}-amine

EXAMPLES 973-983

The following compounds are synthesized as previously described
using 4-amino-1-propanol as a starting material and performing the displacement on
the chloromethyl intermediate with commercially available secondary amines.

Example	Name
973	[4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-dimethyl-amine
974	diethyl-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4]oxazepan-2-ylmethyl}-amine
975	{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-dimethyl-amine
976	{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-diethyl-amine
977	diethyl-{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-amine
978	{4-[2-(5-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-diethyl-amine
979	diethyl-{4-[2-(5-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-amine
980	diethyl-{4-[2-(5-phenoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-amine
981	{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-
	[1,4]oxazepan-2-ylmethyl}-isopropyl-methyl-amine
982	3-[6-(2-azetidin-1-ylmethyl-[1,4]oxazepan-4-yl)-1H-benzoimidazol-
	2-yl]-6-fluoro-1H-indazole
983	6-fluoro-3-[6-(2-pyrrolidin-1-ylmethyl-[1,4]oxazepan-4-yl)-1H-
	benzoimidazol-2-yl]-1H-indazole

EXAMPLE 984

3-[6-((3S)-3,4-Dimethylpiperazinyl)benzimidazol-2-yl]-6-fluoro-1H-indazole Synthesis of (3S)-3-Methylpiperazine-1-carboxylic acid tert-butyl ester

5

To a stirred solution of (2S)-2-methylpiperazine (2 equivalents) in dichloromethane at -10°C, di-tert-butyl dicarbonate (1 equivalent) was added. The mixture was stirred at -10°C for two minutes, and subsequently quenched with saturated aqueous NaHCO₃. The two phases were separated, and the organic layer

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was extracted with methylene chloride. The organic extracts were collected, dried over Na₂SO₄, and concentrated to give the desired product. LC/MS (m/z) 201.0 (MH +), R₁ 1.67 minutes.

Synthesis of (2S)-1,2-Dimethyl-piperazine

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(3S)-3-Methylpiperazine-1-carboxylic acid tert-butyl ester (1 equivalent) and paraformaldehyde (5 equivalents) were dissolved in a mixture of MeOH and AcOH (5:1) on molecular sieves. NaCNBH₃ (4 equivalents) was added to the suspension at 25°C. The slurry was subsequently heated to 80°C. After 10 hours, the mixture was cooled, filtered, and concentrated. The residue was dissolved in dichloromethane and washed with saturated aqueous NaHCO₃. The organic solution was dried (Na₂SO₄), and concentrated. The tert-butoxycarbonyl group was removed by treating the crude amine with saturated HCl in MeOH at room temperature for 30 minutes. The mixture was then concentrated and excess HCl was removed in-vacuo. The desired (2S)-1,2-dimethylpiperazine was thus obtained as the bis HCl salt. LC/MS (m/z) 115.0 (MH+), R₁ 0.33 minutes.

Synthesis of 5-(3S)-(3,4-Dimethyl-piperazin-1-yl)-2-nitro-phenylamine

$$H_2N$$
 N
 N

The title compound was prepared from (2S)-1,2-dimethylpiperazine using the procedure described in Method 8 Step 5. LC/MS (m/z) 251.3 (MH+), R₁ 1.48 minutes.

Synthesis of 4-(3S)-(3,4-Dimethyl-piperazin-1-yl)-benzene-1,2-diamine

$$H_2N$$
 H_2N
 N
 N

5

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The title compound was prepared by reducing 5-(3S)-(3,4-dimethyl-piperazin-1-yl)-2-nitro-phenylamine using the procedure described in Method 8 Step 6.

$Synthesis\ of\ 3\hbox{-}[6\hbox{-}(3S)\hbox{-}(3,4\hbox{-}Dimethyl\hbox{-}piperazin\hbox{-}1\hbox{-}yl)\hbox{-}1H\hbox{-}benzoimidazol\hbox{-}2\hbox{-}yl]\hbox{-}6\hbox{-}fluoro\hbox{-}1H\hbox{-}indazole$

The title compound is synthesized from 4-(3S)-(3,4-dimethyl-piperazin-1-yl)-benzene-1,2-diamine using the procedure described in Example 4.

EXAMPLES 985-988

The following compounds are synthesized as previously described using of 4-(3S)-(3,4-dimethyl-piperazin-1-yl)-benzene-1,2-diamine.

Example	Name
985	5-chloro-3-[6-(3S)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
986	6-chloro-3-[6-(3S)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
987	3-[6-(3S)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-methoxy-1H-indazole
988	3-[6-(3S)-(3,4-Dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-fluoro-1H-indazole

EXAMPLES 989-993

The following compounds are synthesized as previously described in Example 984 starting from (2R)-2-methylpiperazine.

Example	Name
989	5-chloro-3-[6-(3R)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
990	6-chloro-3-[6-(3R)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
991	3-[6-(3R)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-6-fluoro-1H-indazole
992	3-[6-(3R)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-fluoro-1H-indazole
993	3-[6-(3R)-(3,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-methoxy-1H-indazole

EXAMPLE 994

6-Chloro-3-[6-((2S)-2-methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

Synthesis of tert-Butyl (3S)-4-(3-amino-4-nitrophenyl)-3-

5 methylpiperazinecarboxylate

$$O_2N$$
 H_2N
 N
 N

The title compound was synthesized as described in Method 8 Step 5 from tert-butyl (3S)-3-methylpiperazine carboxylate (see Example 984). LC/MS (m/z) 281.3 (MH+), $R_1 2.90$ minutes.

10 Synthesis of tert-butyl (3S)-4-(3,4-diaminophenyl)-3-methylpiperazinecarboxylate

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The title compound is synthesized as described in Method 8 Step 6 using tert-butyl (3S)-4-(3-amino-4-nitrophenyl)-3-methylpiperazinecarboxylate.

Synthesis of 6-Chloro-3-[6-((2S)-2-methylpiperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

The title compound is synthesized from (3S)-4-(3,4-diaminophenyl)3-methylpiperazinecarboxylate using the procedure described in Example 4. The
tert-butoxycarbonyl protecting groups is removed by treatment with saturated HCl in
MeOH.

EXAMPLE 995

3-[6-((2S)-2,4-dimethylpiperazinyl)benzimidazol-2-yl]-6-chloro-1H-indazole

Synthesis of 3-[6-((2S)-2,4-dimethylpiperazinyl)benzimidazol-2-yl]-6-chloro-1H-indazole

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3-[6-((2S)-2-methylpiperazinyl)benzimidazol-2-yl]-6-chloro-1H-indazole (1 equivalent) is dissolved in a mixture of MeOH and acetic acid (10:1), on molecular sieves. Paraformaldehyde (10 equivalents) is added in one portion. The reaction mixture is stirred at room temperature overnight then solid NaCNBH3 is added in small portions. The reaction mixture is refluxed for 5 hours, cooled to room temperature, filtered, and concentrated under reduced pressure. The residue is dissolved in dichloromethane and washed with saturated aqueous NaHCO3. The organic solution is dried over Na2SO4, and the solvent removed under reduced pressure to afford the desired product.

EXAMPLES 996-1005

The following compounds are synthesized from: 3-[6-((2S)-2-methylpiperazinyl)benzimidazol-2-yl]-6-chloro-1H-indazole and 3-[6-((2R)-2-methylpiperazinyl)benzimidazol-2-yl]-6-chloro-1H-indazole according to the procedures described above in examples 994 and 995.

Example	Name Name
996	6-chloro-3-[6-((2S)-4-ethyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
997	6-chloro-3-[6-((2S)-4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
998	6-chloro-3-[6-((2S)-4-cyclobutyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
999	6-chloro-3-[6-((2R)-2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1000	6-chloro-3-[6-((2R)-4-ethyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1001	6-chloro-3-[6-((2R)-4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1002	6-chloro-3-[6-((2R)-4-cyclobutyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1003	6-fluoro-3-[6-((2S)-4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1004	5-chloro-3-[6-((2S)-4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1005	3-[6-((2S)-4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-5-methoxy-1H-indazole

EXAMPLE 1006

 $(\{4\hbox{-}[2\hbox{-}(6\hbox{-}Fluoro(1H\hbox{-}indazol\hbox{-}3\hbox{-}yl))benzimidazol\hbox{-}6\hbox{-}yl]\hbox{-}1\hbox{-}methylpiperazin\hbox{-}2\hbox{-}yl\}methyl) dimethylamine}$

5 Synthesis of 1,4-Bisbenzyl-2-(chloromethyl)piperazine

The title compound was synthesized as previously described in U.S. Patent No. 4,940,710 incorporated herein by reference.

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Synthesis of {[1,4-Bisbenzylpiperazin-2-yl]methyl}dimethylamine

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A mixture of 1,4-bisbenzyl-2-(chloromethyl)piperazine (1 equivalent) and dimethylamine (5 equivalents) in ethanol, was heated at 150°C for 36 hours in a sealed high pressure vessel. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was taken up in 1 N HCl, and the solution was washed with CH₂Cl₂. The water phase was made basic with a 30% aqueous NaOH solution (pH=12) and extracted with CH₂Cl₂. The organic extracts were collected and dried over Na₂SO₄. Evaporation of the solvent under reduced pressure afforded {[1,4-bisbenzylpiperazin-2-yl]methyl}dimethylamine. LC/MS (m/z): 324.3 (MH+), R₁ 1.76 minutes.

Synthesis of Dimethyl(piperazin-2-ylmethyl)amine

{[1,4-bisbenzylpiperazin-2-yl]methyl}dimethylamine (1 equivalent), was dissolved in EtOH and the solution was transferred to a stainless steel high pressure vessel equipped with a pressure gauge. 10% Pd/C was added (10 wt.%), and the vessel charged with H₂. The reaction mixture was stirred at 130°C and 200 psi of H₂ overnight. The reaction mixture was cooled to room temperature, filtered over a pad of Celite, and then evaporated. The desired amine was obtained in quantitative yield as a pale yellow oil. GC/MS: 143 (10%, M+), R₁= 14.3 minutes.

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Synthesis of tert-butyl 3-[(dimethylamino)methyl]piperazine-carboxylate

The title compound was synthesized from dimethyl(piperazin-2-ylmethyl)amine using the procedure described in example 984. GC/MS: 170 (20%, M+-tBuO), R_1 = 13.5 minutes.

Synthesis of Dimethyl[(1-methylpiperazin-2-yl)methyl]amine

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The title compound was synthesized from tert-butyl 3[(dimethylamino)methyl]piperazinecarboxylate using the procedure described in
example 984. Purification by column chromatography on silica gel afforded the Boc
protected amine which was treated with HCl in MeOH to afford the desired product.
LC/MS (m/z): 158.1 (MH+), R₁ 0.27 minutes.

Synthesis of {[4-(3-amino-4-nitrophenyl)-1-methylpiperazin-2-yl]methyl}dimethylamine

The title compound was synthesized from dimethyl[(1-methylpiperazin-2-yl)methyl]amine using the procedure described in Method 8 Step 5. LC/MS (m/z): 294.1 (MH+), Rt 1.11 minutes.

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Synthesis of {[4-(3,4-diaminophenyl)-1-methylpiperazin-2-yl]methyl}dimethylamine

The title compound is synthesized from {[4-(3-amino-4-nitrophenyl)-5 1-methylpiperazin-2-yl]methyl}dimethylamine using the procedure described in Method 8 Step 6.

 $Synthesis \ of \ (\{4-[2-(6-fluoro(1H-indazol-3-yl))benzimidazol-6-yl]-1-methylpiperazin-2-yl\} methyl) dimethylamine$

The title compound is synthesized from {[4-(3,4-diaminophenyl)-1-10 methylpiperazin-2-yl]methyl}dimethylamine using the procedure described in Example 4.

EXAMPLES 1007-1012

The following compounds are synthesized according to the procedure described above in Example 1006.

Example	Name
1007	{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-1-methyl-piperazin-2-ylmethyl}-dimethyl-amine
1008	{4-[2-(5-methoxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-1-methyl-piperazin-2-ylmethyl}-dimethyl-amine
1009	{4-[2-(5-benzyloxy-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-1-methyl-piperazin-2-ylmethyl}-dimethyl-amine
1010	{4-[2-(6-chloro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-1-ethyl-piperazin-2-ylmethyl}-dimethyl-amine
1011	Diethyl-{4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-1-methyl-piperazin-2-ylmethyl}-amine
1012	Diethyl-{1-ethyl-4-[2-(6-fluoro-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-piperazin-2-ylmethyl}-amine

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EXAMPLE 1013

3-(6-(1,4-Diazaperhydroepinyl)benzimidazol-2-yl)-6-fluoro-1H-indazole

Synthesis of tert-Butyl 4-(3-amino-4-nitrophenyl)-1,4-diazaperhydroepinecarboxylate

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The title compound is synthesized from commercially available Bochomopiperazine according to the procedure described in Method 1.

Synthesis of 3-(6-(1,4-Diazaperhydroepinyl)benzimidazol-2-yl)-6-fluoro-1H-indazole

The title compound is synthesized from tert-butyl 4-(3-amino-4-nitrophenyl)-1,4-diazaperhydroepinecarboxylate after the nitro group has been reduced according to the procedure described in Example 4. The tert-butoxycarbonyl is removed treating with saturated HCl in MeOH.

EXAMPLE 1014

15 6-Fluoro-3-[6-(4-methyl(1,4-diazaperhydroepinyl))benzimidazol-2-yl]-1H-indazole

Synthesis of 6-Fluoro-3-[6-(4-methyl(1,4-diazaperhydroepinyl))-benzimidazol-2-yl]-1H-indazole

The title compound is synthesized from 3-(6-(1,4-diazaperhydro-20 epinyl)benzimidazol-2-yl)-6-fluoro-1H-indazole according to the procedure in Examples 984 and 985.

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EXAMPLES 1015-1018

The following compounds are synthesized according to the procedure described above in Example 1014 using an appropriate carbonyl compound.

Example	Name
1015	6-Fluoro-3-[6-(4-ethyl(1,4-diazaperhydroepinyl))-benzimidazol-2-yl]-1H-indazole
1016	6-Fluoro-3-[6-(4-isopropyl(1,4-diazaperhydroepinyl))-benzimidazol-2-yl]-1H-indazole
1017	6-Fluoro-3-[6-(4-cyclobutyl(1,4-diazaperhydroepinyl))-benzimidazol-2-yl]-1H-indazole

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EXAMPLE 1019

2-(6-Fluoro(1H-indazol-3-yl))-6-(1-methyl(3-piperidyloxy))-benzimidazole

Synthesis of 4-(1-Methyl-3-piperidyloxy)phenylamine

KHMDS (1.1 equivalent) was added to a THF solution of 1-

methylpiperidin-3-ol (1 equivalent) at 0°C and stirred until H2 evolution ceased. 1-10 fluoro-4-nitrobenzene (1 equivalent) was then added and the solution was allowed to warm to room temperature. After 2 hours, water was added and the mixture was extracted with EtOAc (3x). The combined organic extracts were dried over Na₂SO₄, and concentrated in vacuo to give a bright yellow oil which was directly used in the reduction step. The oil (1 equivalent) and a catalytic amount of 10% 15 Pd/C were suspended in anhydrous EtOH at room temperature. The reaction flask was evacuated and subsequently filled with H2. After stirring for 18 hours, the mixture was filtered through Celite, and the solvent was concentrated in vacuo to yield 4-(1-methyl-3-piperidyloxy)phenylamine. LC/MS (m/z) 207.2 (MH+), R₁ 0.47 minutes.

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Synthesis of N-[4-(1-Methyl-3-piperidyloxy)phenyl]acetamide

4-(1-methyl-3-piperidyloxy)phenylamine (1 equivalent) was dissolved in CH₂Cl₂ and a catalytic amount of DMAP was added. Acetic anhydride (1.3 equivalents) was added slowly, and the solution was stirred at room temperature overnight. The reaction was then quenched with water and the aqueous layer was extracted with CH₂Cl₂ (3x). The combined organic extracts were dried over Na₂SO₄ and concentrated in vacuo, to yield N-[4-(1-methyl-3-piperidyloxy)phenyl]acetamide as a yellow oil. LC/MS (m/z) 249.3 (MH+), R₁ 1.24 minutes.

10 Synthesis of N-[4-(1-Methyl(3-piperidyloxy))-2-nitrophenyl]-acetamide

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A mixture of HNO₃/H₂SO₄ (1:1, 60% HNO₃:concentrated H₂SO₄) cooled to 0°C was added dropwise to N-[4-(1-methyl-3-piperidyloxy)phenyl]-acetamide to form a 0.16 M solution. The solution was stirred at 0°C for 10 minutes and then at room temperature for 30 minutes. The solution was then diluted with water and made basic (pH=10) with 6 N NaOH. The mixture was then extracted with CH₂Cl₂ (5x), dried over Na₂SO₄, and concentrated *in vacuo* to yield N-[4-(1-methyl(3-piperidyloxy))-2-nitrophenyl]acetamide. LC/MS (m/z) 294.0 (MH+), R₁ 1.24 minutes.

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Synthesis of 4-(1-Methyl(3-piperidyloxy))-2-nitrophenylamine

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N-[4-(1-methyl(3-piperidyloxy))-2-nitrophenyl]acetamide was dissolved in 1:1 MeOH: 6N NaOH (aq) solution (0.03 M). After stirring at room temperature for 2 hours, MeOH was removed *in vacuo*. The remaining solution was extracted with EtOAc (3x). The combined organic extracts were then dried over Na₂SO₄ and concentrated *in vacuo* to give 4-(1-methyl(3-piperidyloxy))-2-nitrophenylamine.

Synthesis of 4-(1-Methyl-3-piperidyloxy)benzene-1,2-diamine

The title compound is synthesized from 4-(1-methyl(3-piperidyloxy))-2-nitrophenylamine using the procedure described in Method 1.

Synthesis of 2-(6-fluoro(1H-indazol-3-yl))-6-(1-methyl(3-piperidyloxy))benzimidazole

15 The title compound is synthesized from 4-(1-Methyl-3-piperidyloxy)benzene-1,2-diamine using the procedure described in Example 4.

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EXAMPLES 1020-1023

The following compounds are synthesized according to the procedure described above in Example 1019.

Example	Name
1020	6-chloro-3-[6-(1-methyl-piperidin-3-yloxy)-1H-benzoimidazol-2-yl]-1H-indazole
1021	5-methoxy-3-[6-(1-methyl-piperidin-3-yloxy)-1H-benzoimidazol-2-yl]-1H-indazole
1022	5-benzyloxy-3-[6-(1-methyl-piperidin-3-yloxy)-1H-benzoimidazol-2-yl]-1H-indazole
1023	3-[6-(1-methyl-piperidin-3-yloxy)-1H-benzoimidazol-2-yl]-1H-5,7-dioxa-1,2-diaza-s-indacene

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EXAMPLE 1024

[2-(1H-Indazol-3-yl)-3H-benzoimidazol-5-yl]-methyl-amine

Synthesis of N¹-Methyl-4-nitro-benzene-1,3-diamine

The title compound was synthesized according to the procedure described in Method 1. LC/MS (m/z) 168.3 (MH+), Rt 1.78 minutes.

Synthesis of N⁴-Methylbenzene-1,2,4-triamine

The title compound is synthesized by reducing N¹-methyl-4-nitrobenzene-1,3-diamine using the procedure described above in Method 8 Step 6.

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Synthesis of [2-(1H-Indazol-3-yl)-3H-benzoimidazol-5-yl]-methyl- amine

The title compound is synthesized from N⁴-methylbenzene-1,2,4-triamine using the procedure described above in Example 4.

EXAMPLES 1025-1033

The following nitroaniline compounds were synthesized according to the procedure described above in Example 1024 starting from the appropriate commercially available amine. The spirocyclic materials used to prepare some of the examples in the following table were synthesized using the procedure following the table.

Example	Name	LC/MS (m/z) (MH+)	R _t (minutes)
1025	N¹-(2-dimethylamino-1-methyl-ethyl)-4-nitro- benzene-1,3-diamine	239.4	1.53
1026	4-nitro-N¹-(2-piperidin-1-yl-ethyl)-benzene- 1,3-diamine	265.1	1.45
1027	N¹-(1-benzyl-piperidin-4-yl)-4-nitro-benzene- 1,3-diamine	294.5	1.71
1028	N¹-(1-ethyl-pyrrolidin-3-ylmethyl)-4-nitro- benzene-1,3-diamine	265.1	1.39
1029	N ¹ -[3-(4-methyl-piperazin-1-yl)-propyl]-4- nitro-benzene-1,3-diamine	294.5	1.38
1030	N¹-methyl-N¹-(1-methyl-piperidin-4-yl)-4- nitro-benzene-1,3-diamine	265.1	1.40
1031	N¹-(2-dimethylamino-ethyl)-N¹-methyl-4- nitro-benzene-1,3-diamine	239.2	1.48
1032	5-(9-isopropyl-1-oxa-4,9-diaza-spiro[5.5]undec-4-yl)-2-nitro-phenylamine	335.3	1.87
1033	5-(2-isopropyl-5-oxa-2,8-diaza-spiro[3.5]non-8-yl)-2-nitro-phenylamine	309.1	1.60

Preparation of Spirocycle Nitroanilines

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The spirocyclic nitroanilines of Examples 1032 and 1033 were synthesized according to the following procedure. The synthesis of Example 1033 is provided below. The synthesis of Example 1032 was carried out in an analogous manner starting from 5-oxa-2,8-diaza-spiro[3.5]nonan-7-one.

5 Synthesis of 9-Isopropyl-1-oxa-4,9-diaza-spiro[5.5]undecan-3-one

1-Oxa-4,9-diaza-spiro[5.5]undecan-3-one was dissolved in MeOH and treated with acetone (6 equivalents) and NaCNBH3 (4 equivalents). To the reaction mixture was added acetic acid (3 equivalents). The reaction was heated at 50°C for 6 hours and then cooled to room temperature. The reaction was then poured into an aqueous NaHCO3 solution and extracted with EtOAc (3x). The combined fractions were dried over MgSO4 and concentrated to provide the title compound as a yellow oil that was purified by chromatography (10% MeOH/CH2Cl2). LC/MS (m/z) 213.1 (MH+), Rt = 1.38 minutes.

15 Synthesis of 9-Isopropyl-1-oxa-4,9-diaza-spiro[5.5]undecane

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9-Isopropyl-1-oxa-4,9-diaza-spiro[5.5]undecan-3-one was dissolved in THF and LiAlH₄ (5 equivalents) was added. The reaction was heated at reflux for 4 hours and then cooled to room temperature. NaF (20 equivalents) and water (5 equivalents) were added and the reaction was stirred vigorously for 1 hour. The

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resulting precipitate was filtered away and the filtrate was concentrated to provide the title compound as a colorless oil. GC/MS (m/z) 198, $R_t = 12.57$ minutes.

Synthesis of 5-(9-Isopropyl-1-oxa-4,9-diaza-spiro[5.5]undec-4-yl)-2-nitrophenylamine

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The title compound was synthesized from 9-isopropyl-1-oxa-4,9-diaza-spiro[5.5]undecane using the procedure described above in Method 2.

Various indazole benzimidazoles are synthesized following the procedure of Example 4 using the nitroanilines of Examples 1024-1033 in combination with a indazole-3-carbaldehyde of formula XVI where R¹, R², R³, and R⁴ have any of the values described above. For example, various indazole benzimidazoles are synthesized by reacting the nitroanilines of Examples 1024-1033 with 5-fluoroindazole, 5-chloroindazole, 6-fluoroindazole, 6-chloroindazole, 5-methoxyindazole, 6-methoxyindazole, 5-ethoxyindazole, and 6-ethoxyindazole 3-carbaldehydes.

Indazole benzimidazole compounds prepared from the nitroanilines of Examples 1024-1029 are reacted with an acyl halide such as acetyl chloride to provide benzimidazole indazoles with an amide group. In an acetylation procedure, a DMA solution of an indazole benzimidazole (1 equivalent) prepared from a nitroaniline of Examples 1024-1029 is added to a room temperature solution of acetyl chloride (1.5 equivalents) in THF over 15 minutes. After this time,

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triethylamine (4 equivalents) is added dropwise and the reaction mixture is stirred for 2 hours at room temperature. The reaction is then partitioned between EtOAc and water. Aqueous layers are extracted with EtOAc (2x) and the combined extractions are washed with water once. Drying over anhydrous MgSO₄ and concentration provides an oil that is purified by reverse phase HPLC to provide the desired product.

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Indazole benzimidazole compounds prepared from the nitroanilines of Examples 1024-1029 are reacted with an acyl halide such as bromoacetyl chloride to provide benzimidazole indazoles with an amide group that includes a bromide for further reaction. In such an acetylation procedure, a DMA solution of an indazole benzimidazole (1 equivalent) prepared from a nitroaniline of Examples 1024-1029 is added to a room temperature solution of bromoacetyl chloride (1.5 equivalents) in THF over 15 minutes. After this time, triethylamine (4 equivalents) is added dropwise and the reaction mixture is stirred for 2 hours at room temperature. The reaction is then partitioned between EtOAc and water. Aqueous layers are extracted with EtOAc (2x) and the combined extractions are washed with water once. Drying over anhydrous MgSO4 and concentration provides an oil that is purified by reverse phase HPLC to provide the desired product.

An indazole benzimidazole compound that has been reacted with a

20 bromoacetyl chloride such as described in the preceding paragraph is further
functionalized by reaction with an amine. In such a reaction, the bromoacetylated
product resulting from the reaction of the bromoacetyl chloride with an indazole
benzimidazole prepared from the nitroanilines of Examples 1024-1029 is suspended
in a desired amine such as, but not limited to, N-methylpiperazine, morpholine, and
25 piperidine and the reaction is heated at reflux for 1 hour. The reaction is
concentrated and the residue is purified via reverse phase HPLC to provide the
desired product in which the bromide has been displaced by the amine.

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EXAMPLE 1034

5-Fluoro-3-[5-fluoro-6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

Synthesis of 4-Fluoro-5-(4-isopropyl-piperazin-1-yl)-2-nitro-phenylamine

$$H_2N$$
 N
 F

4,5-Difluoro-2-nitrophenylamine (1.0 equivalent) and N-isopropyl piperazine were heated at 100°C for 3 hours. The solution was then cooled to room temperature and diluted with water. The resulting precipitate was filtered and dried under vacuum to provide title compound product. LC/MS (m/z) 283.2 (MH+), Rt 1.56 minutes.

Synthesis of 4-Fluoro-5-(4-isopropyl-piperazin-1-yl)-benzene-1,2-diamine

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Reduction of 4-fluoro-5-(4-isopropyl-piperazin-1-yl)-2-nitrophenylamine is carried out using the procedures described in Method 1 to afford the title product.

Synthesis of 5-Fluoro-3-[5-fluoro-6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

The title compound was synthesized as described in Example 4 from 4-fluoro-5-(4-isopropyl-piperazin-1-yl)-benzene-1,2-diamine and 5-fluoro-1H-indazole-3-carbaldehyde. LC/MS (m/z) 397.5 (MH+), R₁ 2.78 minutes.

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EXAMPLE 1035

3,5-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

Synthesis of 1H-Indazole-3,5-dicarbaldehyde

5 The title compound was synthesized as described in Example 4 from the commercially available 5-formylindole. LC/MS (m/z) 175.3 (MH+), Rt 1.80 min.

Synthesis of 3,5-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

The title compound was synthesized from 1H-Indazole-3,5
dicarbaldehyde and 1,2-diaminobenzene using the methods described in Example 4
except that an excess of 1,2-diaminobenzene was used. LC/MS m/z 351.2 (MH+),
Rt 2.03 minutes.

EXAMPLE 1036

5-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-15 yl]-1H-indazole

 $Synthesis\ of\ 5-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole$

The title compound was synthesized as described in Example 4 in three steps. First, 1H-indole-5-carbaldehyde is reacted with 1,2-diaminobenzene in toluene and ethanol. The product of the first reaction is then reacted with NaNO₂ in dioxane with aqueous HCl. The 5-benzimidazole 3-carbaldehyde thus obtained is then reacted with 4-(4- methyl -piperazin-1-yl)-benzene-1,2-diamine to produce the title compound. LC/MS m/z 449.3 (MH+), R₁ 1.71 minutes.

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EXAMPLE 1037

1'-[2-(4-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

Synthesis of 4-Ethoxymethyl-1H-indole

Indole-4-methanol (1.0 equivalent) in THF is added to NaH (1.2 equivalents) in THF at 0°C. EtBr (5.0 equivalents) is added, and the resulting solution is warmed to room temperature and then heated at 50°C for 9 hours. The reaction mixture is quenched with H₂O, extracted with EtOAc. The organic layer is dried over Na₂SO₄, filtered and concentrated. The organic layer is dried over Na₂SO₄, filtered, and concentrated. The product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the desired indole ether title compound.

Synthesis of 4-Ethoxymethyl-1H-indazole-3-carbaldehyde

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The formation of 4-ethoxymethyl-1H-indazole-3-carbaldehyde from 4-ethoxymethyl-1H-indole is carried out as described in Example 4.

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Synthesis of 1'-[2-(4-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

The title compound is formed by reaction of 4-ethoxymethyl-1H-indazole-3-carbaldehyde with 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine and is carried out as described in Example 4.

EXAMPLES 1038-1046

The following compounds are synthesized according to the procedure described above in Example 1037 using the appropriate starting materials.

Example	Name
1038	{4-[2-(4-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1039	{4-[2-(4-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1040	{4-[2-(4-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1041	4-methoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1042	4-benzyloxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1043	4-isopropoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1044	1'-[2-(4-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1045	1'-[2-(4-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1046	1'-[2-(4-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

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EXAMPLE 1047

1'-[2-(5-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

Synthesis of 5-Ethoxymethyl-1H-indole

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Indole-5-methanol (1.0 equivalent) in THF is added to NaH (1.2 equivalents) in THF at 0°C. EtBr (5.0 equivalents) is added, and the resulting solution is warmed to room temperature and then heated at 50°C for 9 hours. The reaction mixture is then quenched with H₂O, extracted with EtOAc. The organic layer is dried over Na₂SO₄, filtered and concentrated. The product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the desired indole ether title compound.

Synthesis of 5-Ethoxymethyl-1H-indazole-3-carbaldehyde

15

The formation of 5-ethoxymethyl-1H-indazole-3-carbaldehyde from 5-ethoxymethyl-1H-indole is carried out as described in Example 4.

Synthesis of 1'-[2-(5-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

The title compound is formed by reaction of 5-ethoxymethyl-1Hindazole-3-carbaldehyde with 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine and is
carried out as described in Example 4.

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EXAMPLES 1048-1056

The following compounds are synthesized according to the procedure described above in Example 1047 using the appropriate starting materials.

Example	Name
1048	{4-[2-(5-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1049	{4-[2-(5-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1050	{4-[2-(5-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1051	5-methoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1052	5-benzyloxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1053	5-isopropoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1054	1'-[2-(5-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1055	1'-[2-(5-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1056	1'-[2-(5-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

EXAMPLE 1057

1'-[2-(6-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]- [1,4']bipiperidinyl

Synthesis of 6-Ethoxymethyl-1H-indole

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Indole-6-methanol (1.0 equivalent) in THF is added to NaH (1.2 equivalents) in THF at 0°C. EtBr (5.0 equivalents) is added, and the resulting solution is warmed to room temperature and then heated at 50°C for 9 hours. The reaction mixture is then quenched with H₂O, extracted with EtOAc. The organic layer is dried over Na₂SO₄, filtered and concentrated. The product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the desired indole ether title compound.

Synthesis of 6-Ethoxymethyl-1H-indazole-3-carbaldehyde

The formation of 6-ethoxymethyl-1H-indazole-3-carbaldehyde from 6-ethoxymethyl-1H-indole is carried out as described in Example 4.

Synthesis of 1'-[2-(6-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

The title compound is formed by reaction of 6-ethoxymethyl-1Hindazole-3-carbaldehyde with 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine and is
carried out as described in Example 4.

EXAMPLES 1058-1066

The following compounds are synthesized according to the procedure described above in Example 1057 using the appropriate starting materials.

Example	Name
1058	{4-[2-(6-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1059	{4-[2-(6-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine

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1060	{4-[2-(6-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1061	6-methoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1062	6-benzyloxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1063	6-isopropoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1064	1'-[2-(6-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1065	1'-[2-(6-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1066	1'-[2-(6-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

EXAMPLE 1067

1'-[2-(7-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

5 Synthesis of 7-Ethoxymethyl-1H-indole

10

Indole-7-methanol (1.0 equivalent) in THF is added to NaH (1.2 equivalents) in THF at 0°C. EtBr (5.0 equivalents) is added, and the resulting solution is warmed to room temperature and then heated at 50°C for 9 hours. The reaction mixture is then quenched with H₂O, extracted with EtOAc. The organic layer is dried over Na₂SO₄, filtered and concentrated. The product is purified by flash chromatography (MeOH:CH₂Cl₂, 5:95) to yield the desired indole ether title compound.

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Synthesis of 7-Ethoxymethyl-1H-indazole-3-carbaldehyde

The formation of 7-ethoxymethyl-1H-indazole-3-carbaldehyde from 7-ethoxymethyl-1H-indole is carried out as described in Example 4.

5 Synthesis of 1'-[2-(7-Ethoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl][1,4']bipiperidinyl

The title compound is formed by reaction of 7-ethoxymethyl-1H-indazole-3-carbaldehyde with 4-[1,4']bipiperidinyl-1'-yl-benzene-1,2-diamine and is carried out as described in Example 4.

10 EXAMPLES 1068-1076

The following compounds are synthesized according to the procedure described above in Example 1067 using the appropriate starting materials.

Example	Name
1068	{4-[2-(7-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1069	{4-[2-(7-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1070	{4-[2-(7-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-5-methyl-morpholin-2-ylmethyl}-dimethyl-amine
1071	7-methoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1072	7-benzyloxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1073	7-isopropoxymethyl-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

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1074	1'-[2-(7-methoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1075	1'-[2-(7-benzyloxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl
1076	1'-[2-(7-isopropoxymethyl-1H-indazol-3-yl)-3H-benzoimidazol-5-yl]-[1,4']bipiperidinyl

EXAMPLE 1077

3-(1H-Benzoimidazol-2-yl)-1H-indazol-4-ol

A solution of 4-hydroxyindole (1.0 equivalent), benzyl chloroformate

(1.1 equivalents), and disopropylethylamine (2.0 equivalents) in CH₂Cl₂ is stirred for 18 hours. The solution is concentrated to yield the desired CBz protected indole ether. The product is then reacted with NaNO₂ in HCl and dioxane as described in Example 4, followed by reaction with phenylenediamine in EtOH and toluene using the methods described above to yield the Cbz protected indazole benzimidazole.

The Chz-protected product is deprotected using 10% Pd/C and H₂ to provide the

10 The Cbz-protected product is deprotected using 10% Pd/C and H₂ to provide the desired 4-hydroxyindole benzimidazole.

EXAMPLE 1078

3-(1H-Benzoimidazol-2-yl)-1H-indazol-6-ol

A solution of 6-hydroxyindole (1.0 equivalent), benzyl chloroformate (1.1 equivalents), and diisopropylethylamine (2.0 equivalents) in CH₂Cl₂ is stirred for 18 hours. The solution is concentrated to yield the desired CBz protected indole ether. The product is then reacted with NaNO₂ in HCl and dioxane as described in Example 4, followed by reaction with phenylenediamine in EtOH and toluene using the methods described above to yield the Cbz protected indazole benzimidazole.

The Cbz-protected product is deprotected using 10% Pd/C and H₂ to provide the desired 6-hydroxyindole benzimidazole.

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EXAMPLE 1079

3-(1H-Benzoimidazol-2-yl)-1H-indazol-7-ol

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A solution of 7-hydroxyindole (1.0 equivalent), benzyl chloroformate (1.1 equivalents), and diisopropylethylamine (2.0 equivalents) in CH₂Cl₂ is stirred for 18 hours. The solution is concentrated to yield the desired CBz protected indole ether. The product is then reacted with NaNO₂ in HCl and dioxane as described in Example 4, followed by reaction with phenylenediamine in EtOH and toluene using the methods described above to yield the Cbz protected indazole benzimidazole. The Cbz-protected product is deprotected using 10% Pd/C and H₂ to provide the desired 7-hydroxyindole benzimidazole.

EXAMPLES 1080-1095

The following compounds are synthesized according to the procedures described above using the appropriate starting materials.

Example	. Name
1080	3-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-ol
1081	3-[5-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-ol
1082	3-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-ol
1083	3-[5-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-4-ol
1084	3-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-ol
1085	3-[5-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-ol
1086	3-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-ol
1087	3-[5-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-ol

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1088	3-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-ol
1089	3-[5-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-ol
1090	3-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-ol
1091	3-[5-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-6-ol
1092	3-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ol
1093	3-[5-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ol
1094	3-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ol
1095	3-[5-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-7-ol

EXAMPLE 1096

$\label{thm:condition} 5-[5-(4-Methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole$

The synthesis of the title compound is carried out using 1H-indazole-3,5-dicarbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine and the methods described in Example 4 except that an excess of the 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine is used.

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EXAMPLE 1097

5-(1H-Benzoimidazol-2-yl)-3-[6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

Synthesis of 5-(1H-Benzoimidazol-2-yl)-3-[6-(4-isopropyl-piperazin-1-yl)-1H-5 benzoimidazol-2-yl]-1H-indazole

The synthesis of the title compound is carried out as described in Example 1036 from 4-(4-isopropyl-piperazin-1-yl)-benzene-1,2-diamine to produce the title compound.

EXAMPLES 1098-1106

The following compounds are synthesized according to the procedures described above using the appropriate starting materials.

Example	Name
1098	[4-(2-{3-[6-(2-dimethylaminomethyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazol-5-yl}-1H-benzoimidazol-5-yl)-5-methyl-morpholin-2-ylmethyl]-dimethyl-amine
1099	5-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-3-[6-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1100	3-(1H-benzoimidazol-2-yl)-5-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1101	5-[5-(4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-3-[6-(4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1102	(4-{2-[5-(1H-benzoimidazol-2-yl)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-amine
1103	3-(1H-benzoimidazol-2-yl)-5-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1104	5-(1H-benzoimidazol-2-yl)-3-[6-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1105	5-(1H-benzoimidazol-2-yl)-3-[6-(4-isopropyl-2-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

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	1106	(4-{2-[3-(1H-benzoimidazol-2-yl)-1H-indazol-5-yl]-1H-
		benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-
i		amine

EXAMPLE 1107

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3,4-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

Synthesis of 1H-Indazole-3,4-dicarbaldehyde

The commercially available 1H-indole-4-carbaldehyde is reacted with NaNO2 in the presence of HCl and H2O in dioxane to produce the title compound.

Synthesis of 3,4-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

The title compound is prepared using the procedure described in

Example 4 from 1H-indazole-3,4-dicarbaldehyde and an excess of 1,2diaminobenzene.

EXAMPLE 1108

 $\label{lem:condition} \mbox{4-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole}$

15 Synthesis of 4-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

The synthesis of the title compound is carried out as described in 1036 from 4-benzimidazole-3-indazole carbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine to produce the title compound.

EXAMPLES 1109-1115

The following compounds are synthesized according to the procedures described above in Example 1108 using the appropriate starting materials.

Example	Name
1109	4-(1H-benzoimidazol-2-yl)-3-[6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1110	4-(1H-benzoimidazol-2-yl)-3-[6-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1111	(4-{2-[4-(1H-benzoimidazol-2-yl)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-amine
1112	3-(1H-benzoimidazol-2-yl)-4-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1113	3-(1H-benzoimidazol-2-yl)-4-[6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1114	3-(1H-benzoimidazol-2-yl)-4-[6-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1115	(4-{2-[3-(1H-benzoimidazol-2-yl)-1H-indazol-4-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethylamine

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EXAMPLE 1116

3,6-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

Synthesis of 1H-Indazole-3,6-dicarbaldehyde

The synthesis of the title compound is carried out from 1H-indole-6-carbaldehyde by reacting it with NaNO2 in dioxane with aqueous HCl using the method described in Example 4.

Synthesis of 3,6-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

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The synthesis of the title compound is carried out from 1H-Indazole-3,6-dicarbaldehyde by reacting it with an excess of 1,2-diaminobenzene using the method described in Example 4.

EXAMPLE 1117

6-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

 $Synthesis\ of\ 6-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole$

The synthesis of the title compound is carried out as described in 1036 from 6-benzimidazole-3-indazole carbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine to produce the title compound.

EXAMPLES 1118-1124

The following compounds are synthesized according to the procedures described above in Example 1108 using the appropriate starting materials.

Example	Name
1118	6-(1H-benzoimidazol-2-yl)-3-[6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1119	6-(1H-benzoimidazol-2-yl)-3-[6-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1120	(4-{2-[6-(1H-benzoimidazol-2-yl)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethyl-amine

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1121	3-(1H-benzoimidazol-2-yl)-6-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1122	3-(1H-benzoimidazol-2-yl)-6-[5-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1123	3-(1H-benzoimidazol-2-yl)-6-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1124	3-(1H-benzoimidazol-2-yl)-6-[5-(2-isobutyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazole

EXAMPLE 1125

3,7-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

Synthesis of 1H-Indazole-3,7-dicarbaldehyde

The synthesis of the title compound is carried out from 1H-indole-7-carbaldehyde by reacting it with NaNO2 in dioxane with aqueous HCl using the method described in Example 4.

Synthesis of 3,7-Bis-(1H-benzoimidazol-2-yl)-1H-indazole

The synthesis of the title compound is carried out from 1H-indazole-3,7-dicarbaldehyde by reacting it with an excess of 1,2-diaminobenzene using the method described in Example 4.

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EXAMPLE 1126

7-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

Synthesis of 7-(1H-Benzoimidazol-2-yl)-3-[6-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole

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The synthesis of the title compound is carried out as described 1036 from 7-benzimidazole-3 indazolecarbaldehyde and 4-(4-methylpiperazin-1-yl)-benzene-1,2-diamine to produce the title compound.

EXAMPLES 1127-1133

The following compounds are synthesized according to the procedures described above in Example 1108 using the appropriate starting materials.

Example	Name
1127	7-(1H-benzoimidazol-2-yl)-3-[6-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1128	7-(1H-benzoimidazol-2-yl)-3-[6-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1129	(4-{2-[7-(1H-benzoimidazol-2-yl)-1H-indazol-3-yl]-3H-benzoimidazol-5-yl}-5-methyl-morpholin-2-ylmethyl)-dimethylamine
1130	3-(1H-benzoimidazol-2-yl)-7-[5-(4-methyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1131	3-(1H-benzoimidazol-2-yl)-7-[5-(4-isopropyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1132	3-(1H-benzoimidazol-2-yl)-7-[5-(2,4-dimethyl-piperazin-1-yl)-1H-benzoimidazol-2-yl]-1H-indazole
1133	3-(1H-benzoimidazol-2-yl)-7-[5-(2-isobutyl-5-methyl-morpholin-4-yl)-1H-benzoimidazol-2-yl]-1H-indazole

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EXAMPLES 1134-1160

Examples 1134-1160 were using the procedure set forth above in Example 732for the synthesis of indazole benzimidazoles.

Example	Name	LC/MS m/z (MH+)
1134	4-{[2-(5-fluoro-1H-indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	417.4
1135	4-{[2-(5-methoxy-1H-indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	429.4
1136	Methyl 3-[1-methyl-5-({2- [(methylamino)carbonyl]pyridin-4-yl}oxy)-1H- benzimidazol-2-yl]-1H-indazole-5-carboxylate	457.5
1137	N-methyl-4-{[1-methyl-2-(5-methyl-1H-indazol-3-yl)-1H-benzimidazol-5-yl]oxy}pyridine-2-carboxamide	413.5
1138	4-({2-[5-(benzyloxy)-1H-indazol-3-yl]-1-methyl-1H-benzimidazol-5-yl}oxy)-N-methylpyridine-2-carboxamide	505.5
1139	4-{[2-(6-fluoro-1H-indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	417.4
1140	4-{[2-(6-chloro-1H-indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	433.9
1141	4-{[2-(5,6-difluoro-1H-indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	435.4
1142	4-{[2-(6-chloro-5-fluoro-1H-indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	451.9
1143	4-{[2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-1-methyl-1H-benzimidazol-5-yl]oxy}-N-methylpyridine-2-carboxamide	443.4
1144	4-{[2-(5-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	419.8
1145	4-{[2-(5-bromo-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	464.3
1146	Methyl 3-[6-({2-[(methylamino)carbonyl]pyridin-4-yl}oxy)-1H-benzimidazol-2-yl]-1H-indazole-5-carboxylate	443.4

1147	N-methyl-4-{[2-(5-methyl-1H-indazol-3-yl)-1H-	399.4
	benzimidazol-6-yl]oxy}pyridine-2-carboxamide	
1148	4-({2-[5-(benzyloxy)-1H-indazol-3-yl]-1H-	491.5
	benzimidazol-6-yl}oxy)-N-methylpyridine-2- carboxamide	
1149	4-{[2-(6-fluoro-1H-indazol-3-yl)-1H-benzimidazol-6-	403.4
	yl]oxy}-N-methylpyridine-2-carboxamide	
1150	4-{[2-(5,6-difluoro-1H-indazol-3-yl)-1H-benzimidazol-	421.4
	6-yl]oxy}-N-methylpyridine-2-carboxamide	
1151	4-{[2-(1H-[1,3]dioxolo[4,5-f]indazol-3-yl)-1H-	429.4
	benzimidazol-6-yl]oxy}-N-methylpyridine-2-	
1152	carboxamide	419.8
1152	4-{[2-(7-chloro-1H-indazol-3-yl)-1H-benzimidazol-6-yl]oxy}-N-methylpyridine-2-carboxamide	419.8
1153	4-{[2-(6-cyano-1H-indazol-3-yl)-1H-benzimidazol-6-	410.4
···	yl]oxy}-N-methylpyridine-2-carboxamide	
1154	4-{[2-(5-isobutoxy-1H-indazol-3-yl)-1H-benzimidazol-	457.5
	6-yl]oxy}-N-methylpyridine-2-carboxamide	
1155	5-fluoro-3-[5-fluoro-6-(4-isopropylpiperazin-1-yl)-1H-	397.4
	benzimidazol-2-yl]-1H-indazole	
1156	3-[5-fluoro-6-(4-isopropylpiperazin-1-yl)-1H-	393.5
	benzimidazol-2-yl]-5-methyl-1H-indazole	
1157	5-(benzyloxy)-3-[5-fluoro-6-(4-isopropylpiperazin-1-yl)-	485.6
	1H-benzimidazol-2-yl]-1H-indazole	
1158	6-fluoro-3-[5-fluoro-6-(4-isopropylpiperazin-1-yl)-1H-	397.4
	benzimidazol-2-yl]-1H-indazole	
1159	6-chloro-3-[5-fluoro-6-(4-isopropylpiperazin-1-yl)-1H-	413.9
	benzimidazol-2-yl]-1H-indazole	
1160	3-[5-fluoro-6-(4-isopropylpiperazin-1-yl)-1H-	423.5
	benzimidazol-2-yl]-1H-[1,3]dioxolo[4,5-f]indazole	

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EXAMPLE 1161

8-[2-(1H-Indazol-3-yl)-1H-benzoimidazol-5-yl]-1,4-dioxa-8-aza-spiro[4.5]decane

Synthesis of 5-(1,4-Dioxa-8-aza-spiro[4.5]dec-8-yl)-2-nitro-phenylamine

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The title compound was synthesized as described in Method 10, Step 2 from 1,4-dioxa-8-aza-spiro[4.5]decane and 5-fluoro-2-nitrophenylamine. LC/MS (m/z) 280.3 (MH+), Rt 2.41 minutes.

Synthesis of 8-[2-(1H-Indazol-3-yl)-1H-benzoimidazol-5-yl]-1,4-dioxa-8-aza-spiro[4.5]decane

5-(1,4-Dioxa-8-aza-spiro[4.5]dec-8-yl)-2-nitro-phenylamine was reduced to produce 4-(1,4-dioxa-8-aza-spiro[4.5]dec-8-yl)-benzene-1,2-diamine using the procedures described above. The reduced 1,2-diaminobenzene product is heated in toluene and EtOH at 100°C overnight with indazole-3-carbaldehyde (1.0 equivalent) to give the title compound.

EXAMPLE 1162

 $\{1-[2-(1H-Indazol-3-yl)-1H-benzoimidazol-5-yl]-piperidin-4-yl\}-dimethyl-amine \\ Synthesis of \{1-[2-(1H-Indazol-3-yl)-1H-benzoimidazol-5-yl]-piperidin-4-yl\}-dimethyl-amine$

The dioxolane protecting group of 8-[2-(1H-indazol-3-yl)-1Hbenzoimidazol-5-yl]-1,4-dioxa-8-aza-spiro[4.5]decane is removed with PPTS (1.15 equivalents) in acetone in the microwave (~300 watts, 150 °C, 11 minutes) to give the ketone. The ketone is reacted with dimethylamine and BH₃:pyridine (10

equivalents) in AcOH:MeOH:CH₂Cl₂ as described in Example 710 to yield the title compound.

EXAMPLES 1163-1199

The following compounds are synthesized according to the procedures described in Examples 1161 and 1162 using the appropriate starting materials.

Example	Name
1163	{1-[2-(5-chloro(1H-indazol-3-yl))benzimidazol-5-yl](4-piperidyl)}dimethylamine
1164	{1-[2-(5-fluoro(1H-indazol-3-yl))benzimidazol-5-yl](4-piperidyl)}dimethylamine
1165	{1-[2-(5-methoxy(1H-indazol-3-yl))benzimidazol-5-yl](4-piperidyl)}dimethylamine
1166	5-chloro-3-[5-(4-pyrrolidinylpiperidyl)benzimidazol-2-yl]-1H-indazole
1167	5-fluoro-3-[5-(4-pyrrolidinylpiperidyl)benzimidazol-2-yl]-1H-indazole
1168	5-methoxy-3-[5-(4-pyrrolidinylpiperidyl)benzimidazol-2-yl]-1H-indazole
1169	{1-[2-(6-chloro(1H-indazol-3-yl))benzimidazol-5-yl](4-piperidyl)}dimethylamine
1170	{1-[2-(6-fluoro(1H-indazol-3-yl))benzimidazol-5-yl](4-piperidyl)}dimethylamine
1171	{1-[2-(6-methoxy(1H-indazol-3-yl))benzimidazol-5-yl](4-piperidyl)}dimethylamine
1172	6-chloro-3-[5-(4-pyrrolidinylpiperidyl)benzimidazol-2-yl]-1H-indazole
1173	6-fluoro-3-[5-(4-pyrrolidinylpiperidyl)benzimidazol-2-yl]-1H-indazole
1174	6-methoxy-3-[5-(4-pyrrolidinylpiperidyl)benzimidazol-2-yl]-1H-indazole
1175	5-chloro-3-{5-[4-(4-methylpiperazinyl)piperidyl]benzimidazol-2-yl}-1H-indazole

1176	5-fluoro-3-{5-[4-(4-methylpiperazinyl)piperidyl]benzimidazol-2-yl}-1H-indazole
1177	5-methoxy-3-{5-[4-(4-methylpiperazinyl)piperidyl]benzimidazol-2-yl}-1H-indazole
1178	4-{1-[2-(5-chloro-1H-indazol-3-yl)benzimidazol-5-yl]-4-piperidyl}morpholine
1179	4-{1-[2-(5-fluoro-1H-indazol-3-yl)benzimidazol-5-yl]-4-piperidyl}morpholine
1180	5-methoxy-3-[5-(4-morpholin-4-ylpiperidyl)benzimidazol-2-yl]-1H-indazole
1181	6-chloro-3-{5-[4-(4-methylpiperazinyl)piperidyl]benzimidazol-2-yl}-1H-indazole
1182	6-fluoro-3-{5-[4-(4-methylpiperazinyl)piperidyl]benzimidazol-2-yl}-1H-indazole
1183	6-methoxy-3-{5-[4-(4-methylpiperazinyl)piperidyl]benzimidazol-2-yl}-1H-indazole
1184	4-{1-[2-(6-chloro-1H-indazol-3-yl)benzimidazol-5-yl]-4-piperidyl}morpholine
1185	4-{1-[2-(6-fluoro-1H-indazol-3-yl)benzimidazol-5-yl]-4-piperidyl}morpholine
1186	6-methoxy-3-[5-(4-morpholin-4-ylpiperidyl)benzimidazol-2-yl]-1H-indazole
1187	{1'-[2-(1H-Indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1188	{1'-[2-(5-chloro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1189	{1'-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1190	{1'-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1191	1'-[2-(5-chloro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]-4-pyrrolidin-1-yl-[1,4']bipiperidinyl
1192	1'-[2-(5-fluoro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]-4-pyrrolidin-1-yl-[1,4']bipiperidinyl

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1193	1'-[2-(5-methoxy-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]-4-pyrrolidin-1-yl-[1,4']bipiperidinyl
1194	{1'-[2-(6-chloro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1195	{1'-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1196	{1'-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]- [1,4']bipiperidinyl-4-yl}-dimethyl-amine
1197	1'-[2-(6-chloro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]-4-pyrrolidin-1-yl-[1,4']bipiperidinyl
1198	1'-[2-(6-fluoro-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]-4-pyrrolidin-1-yl-[1,4']bipiperidinyl
1199	1'-[2-(6-methoxy-1H-indazol-3-yl)-1H-benzoimidazol-5-yl]-4-pyrrolidin-1-yl-[1,4']bipiperidinyl

ASSAY PROCEDURES

In vitro kinase assays for receptor tyrosine kinases

The kinase activity of various protein tyrosine kinases can be 5 measured by providing ATP and a suitable peptide or protein tyrosine-containing substrate, and assaying the transfer of phosphate moiety to the tyrosine residue. Recombinant proteins corresponding to the cytoplasmic domains of the flt-1 (VEGFR1), Flk-1, Tie-2, PDGF, and bFGF receptors were expressed in Sf9 insect cells using a Baculovirus expression system (InVitrogen) and purified via Glu antibody interaction (for Glu-epitope tagged constructs) or by Metal Ion 10 Chromatography (for His6 tagged constructs). For each assay, test compounds were serially diluted in DMSO then mixed with an appropriate kinase reaction buffer plus ATP. Kinase protein and an appropriate biotinylated peptide substrate were added to give a final volume of 50-100 µL, reactions were incubated for 1-3 hours at room temperature and stopped by the addition of 25-50 µL of 45mM EDTA, 50mM 15 Hepes pH 7.5. Stopped reaction mix (75 µL) was transferred to a streptavidin coated microtiter plate (Boehringer Mannheim) and incubated for 1 hour.

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Phosphorylated peptide product was measured with the DELFIA time-resolved fluorescence system (Wallac or PE Biosciences), using a Eu-labeled anti-phosphotyrosine antibody PT66 with the modification that the DELFIA assay buffer was supplemented with 1 mM MgCl₂ for the antibody dilution. Time resolved fluorescence was read on a Wallac 1232 DELFIA fluorometer or a PE Victor II multiple signal reader. The concentration of each compound for 50% inhibition (IC₅₀) was calculated by non-linear regression using XL Fit data analysis software.

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Flt-1, Flk-1, Tie-2, and bFGFR kinases were assayed in 50 mM Hepes pH 7.0, 2 mM MgCl₂, 10 mM MnCl₂, 1 mM NaF, 1 mM DTT, 1 mg/ml BSA, 2 μM ATP, and 0.20-0.50 μM corresponding biotinylated peptide substrate. Flt-1, Flk-1, Tie-2, and bFGFR kinases were added at 0.1 μg/mL, 0.05 μg/mL, or 0.1 μg/mL respectively. For the PDGFR kinase assay, 120 μg/mL enzyme with the same buffer conditions as above was used except for changing ATP and peptide substrate concentrations to 1.4 μM ATP, and 0.25 μM biotin-GGLFDDPSYVNVONL-NH2 peptide substrate.

In vitro kinase assays for serine/threonine kinases

The kinase activity of various protein serine/threonine kinases can be measured by providing ATP and a suitable peptide or protein serine/threonine containing substrate, and assaying the transfer of phosphate moiety to the serine or threonine residue. Recombinant proteins containing the kinase domains of GSK-3, NEK-2, and CHK 1 enzymes were expressed in Sf9 insect cells using a Baculovirus expression system (InVitrogen) and purified via Glu antibody interaction (for Gluepitope tagged constructs) or by Metal Ion Chromatography (for Hisω tagged constructs). The purified cdc 2 enzyme used in the assay is commercially available and was purchased from New England Bio Labs. For each assay, test compounds were serially diluted in DMSO then mixed with an appropriate kinase reaction buffer plus ³²P g-labeled ATP. Kinase protein and an appropriate biotinylated peptide substrate were added to give a final volume of 100 μL. Reactions were incubated for 1-2 hours at room temperature and stopped by the addition of 50 μL

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of a solution of 45 mM EDTA, 50 mM Hepes pH 7.5, 50 μ L unlabelled ATP. Stopped reaction mix (75 μ L) was transferred to a streptavidin coated microtiter plate (Boehringer Mannheim) and incubated for 1 hour. Streptavidin plates were washed with PBS, diluted with 200 μ L Microscint 20 scintillation fluid, sealed, and counted using TopCount. The concentration of each compound for 50% inhibition (ICso) was calculated by non-linear regression using XL Fit data analysis software.

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Each of the compounds produced in Examples 1-728 was synthesized and assayed using the procedures described above. The majority of the exemplary compounds displayed an IC₅₀ value of less than 10 μM with respect to VEGFR1, Flk-1, bFGF, Tie-2, CHK-1, cdc2, GSK-3, NEK-2, and PDGF. In addition, many of the exemplary compounds exhibited IC₅₀ values in the nM range and showed potent activity with respect to VEGFR1, Flk-1, bFGF, Tie-2, CHK-1, cdc2, GSK-3, NEK-2, and PDGF with IC₅₀ values of less than 1 μM. The other examples also exhibited such activity with respect to VEGFR1, Flk-1, bFGF, Tie-2, CHK-1, cdc2, GSK-3, NEK-2, and PDGF or will be shown to exhibit such activity. The exemplary compounds also exhibit inhibition activity with respect to KDR.

Each of Examples 1-728 and many of the other examples exhibited activity in one or more important assays. Many of the other exemplary compounds will be shown to exhibit activity in these assays. For this reason, each of the Exemplary compounds is both individually preferred and is preferred as a group. One, two, or more compounds of the invention may be used in combination in pharmaceutical formulations, medicaments, and in methods of treating subjects. Furthermore, each of the R¹-R¹⁰ groups of the exemplary compounds is preferred individually and as a member of a group.

In one embodiment, the invention provides a method of inhibiting flt
1 (VEGFR1). The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

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In one embodiment, the invention provides a method of inhibiting KDR (VEGFR2). The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

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In one embodiment, the invention provides a method of inhibiting Flk-1. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting bFGFR. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting GSK-3. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting NEK-2. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting CHK-1. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first,

second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting cdc

2. The method includes administering an effective amount of a compound, or a
pharmaceutically acceptable salt thereof, of any of the embodiments of the first,
second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I
to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting Tie-2. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

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In one embodiment, the invention provides a method of inhibiting PDGF. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting bFGF. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

In one embodiment, the invention provides a method of inhibiting a serine/threonine kinase. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

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In one embodiment, the invention provides a method of inhibiting a tyrosine kinase. The method includes administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of any of the embodiments of the first, second, third, fourth, fifth, sixth, and/or seventh groups of compounds of formula I to a subject, such as a human, in need thereof.

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It should be understood that the organic compounds according to the invention may exhibit the phenomenon of tautomerism. As the chemical structures within this specification can only represent one of the possible tautomeric forms, it should be understood that the invention encompasses any tautomeric form of the drawn structure.

It is understood that the invention is not limited to the embodiments set forth herein for illustration, but embraces all such forms thereof as come within the scope of the following claims.

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CLAIMS

What is claimed is:

1 1. A compound having the structure I, a tautomer of the

2 compound, a pharmaceutically acceptable salt of the compound, or a

3 pharmaceutically acceptable salt of the tautomer

I

5 wherein

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 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

7 R¹ is selected from the group consisting of -H, -F, -Cl, and -Br;

8 R^2 is selected from the group consisting of -H, -F, -Cl, -Br, -C \equiv N,

9 -NO₂, -CO₂H, substituted and unsubstituted amino groups, substituted and

unsubstituted alkyl groups, substituted and unsubstituted -C(=0)O-alkyl groups,

11 substituted and unsubstituted -C(=O)O-aryl groups, substituted and unsubstituted

12 -C(=O)O-heteroaryl groups, substituted and unsubstituted -C(=O)N(H)-alkyl 13 groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and 14 unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 15 -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, 16 substituted and unsubstituted -N(H)C(=0)-heterocyclyl groups, substituted and 17 unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted 18 -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted -N(H)-heterocyclyl 19 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 20 arylalkoxy groups, and substituted and unsubstituted heterocyclylalkoxy groups; 21 R³ is selected from the group consisting of -H, -F, -Cl, -Br, and 22 substituted and unsubstituted alkoxy groups; R^4 is -H; 23 24 R⁵ is selected from the group consisting of -H, -F, -Cl, substituted 25 and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, 26 substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino 27 groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N; 28 29 R⁶ is selected from the group consisting of -H, -F, -Cl, -Br, -CF₃, 30 -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted 31 alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, 32 substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including 33 34 substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and 35 unsubstituted arylheterocyclyl groups, and substituted and unsubstituted 36 cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, 37 substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino

38 groups including substituted and unsubstituted dialkylamino groups, substituted and 39 unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted 40 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, 41 and substituted and unsubstituted heterocyclylamino groups; substituted and 42 unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted 43 -C(=O)N(H)-aryl groups, and substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups; or R^6 is absent if Z^2 is N; 44 45 R⁷ is selected from the group consisting of -H, -F, -Cl, -Br, -CF₃, 46 -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted 47 alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted 48 49 alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including 50 substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and 51 unsubstituted arylheterocyclyl groups, and substituted and unsubstituted 52 cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, 53 substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino 54 groups including substituted and unsubstituted dialkylamino groups, substituted and 55 unsubstituted (alkyl)(heterocyclyl)amino groups, and substituted and unsubstituted 56 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, substituted and unsubstituted heterocyclylamino groups; substituted and 57 58 unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted 59 -C(=O)N(H)-aryl groups, and substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups; or R^7 is absent if Z^3 is N; 60 R⁸ is selected from the group consisting of -H, -F, -Cl, substituted 61 62 and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, 63 substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino

groups, substituted and unsubstituted dialkylamino groups, and substituted and

unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

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66 R⁹ is -H; and

67 R^{10} is -H,

and further wherein at least one of R¹, R², R³, R⁵, R⁶, R⁷ or R⁸ is not

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69 -H.

- 1 2. The compound of claim 1, wherein Z^1 , Z^2 , Z^3 , and Z^4 are C.
- 1 3. The compound of claim 1, wherein R¹ is selected from -H, -F,
- 2 -Cl, or -Br.
- 1 4. The compound of claim 1, wherein R³ is selected from the
- 2 group consisting of -F, -Cl, -Br, and substituted and unsubstituted alkoxy groups.
- 1 5. The compound of claim 1, wherein R² is selected from the
- 2 group consisting of -H, -F, -Cl, -CO₂H, substituted and unsubstituted alkyl groups,
- 3 substituted and unsubstituted -C(=0)O-alkyl groups, substituted and unsubstituted
- 4 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 5 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 6 unsubstituted -N(H)C(=0)-alkyl groups, substituted and unsubstituted
- 7 -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl
- 8 groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
- 9 and unsubstituted -N(H)C(=0)N(H)-aryl groups, substituted and unsubstituted
- 10 -N(H)-heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted
- 11 and unsubstituted arylalkoxy groups, and substituted and unsubstituted
- 12 heterocyclylalkoxy groups.
- 1 6. The compound of claim 1, wherein R^2 is H.

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1	7. The compound of claim 1, wherein R ² is an unsubstituted
2	alkoxy group having from 1 to 4 carbon atoms, a substituted or unsubstituted alkyl
3	group, or a substituted or unsubstituted arylalkoxy group
	•
1	8. The compound of claim 1, wherein R ³ is selected from the
2	group consisting of -H, -F, -Cl, and -OMe.
1	9. The compound of claim 1, wherein R ⁵ or R ⁸ is selected from
2	-H, a -CH ₃ group, or a morpholine group.
1	10. The compound of claim 1, wherein R ⁶ is selected from the
2	group consisting of -Br, substituted and unsubstituted alkyl groups, substituted and
3	unsubstituted alkoxy groups including substituted and unsubstituted
4	heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and
5	substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted
6	$-C(=O)N(H) - alkyl \ groups, \ substituted \ and \ unsubstituted \ -C(=O)N(H) - aryl \ groups,$
7	substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
8	unsubstituted heterocyclyl groups including substituted and unsubstituted
9	heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl
10	groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted
11	and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy
12	groups, and substituted and unsubstituted amino groups including substituted and
13	unsubstituted dialkylamino groups, substituted and unsubstituted
14	(alkyl)(heterocyclyl)amino groups, substituted and unsubstituted
15	heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups,

1 11. The compound of claim 1, wherein R⁶ is an alkoxy group

and substituted and unsubstituted heterocyclylamino groups.

2 having from 1-6 carbon atoms or an alkyl group having from 1-6 carbon atoms.

- 1 12. The compound of claim 1, wherein R⁶ is a substituted alkoxy
- 2 group having the formula -OCH₂(CH₂)_mR¹¹ where m is an integer selected from the
- 3 group consisting of 0, 1, and 2 and R¹¹ is selected from the group consisting of
- 4 substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl
- 5 groups, and substituted and unsubstituted heterocyclyl groups.
- 1 13. The compound of claim 1, wherein R⁶ is a substituted amino
- 2 group having the formula -N(R¹²)CH₂(CH₂)_mR¹³ where m is an integer selected from
- 3 0, 1, or 2, R¹³ is selected from the group consisting of substituted and unsubstituted
- 4 alkoxy groups, substituted and unsubstituted aryl groups, and substituted and
- 5 unsubstituted heterocyclyl groups, and R¹² is selected from the group consisting of
- 6 -H, and substituted and unsubstituted alkyl groups.
- 1 14. The compound of claim 1, wherein R⁶ is a substituted or
- 2 unsubstituted heterocyclyl group.
- 1 15. The compound of claim 1, wherein at least one of R^6 or R^7 is
- 2 -H.
- 1 16. The compound of claim 1, wherein R⁷ is selected from the
- 2 group consisting of substituted and unsubstituted alkyl groups, substituted and
- 3 unsubstituted alkoxy groups including substituted and unsubstituted
- 4 heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and
- 5 substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 7 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 8 unsubstituted heterocyclyl groups including substituted and unsubstituted
- 9 heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl
- 10 groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted

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11 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy

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- 12 groups, and substituted and unsubstituted amino groups including substituted and
- 13 unsubstituted dialkylamino groups, substituted and unsubstituted
- 14 (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted
- 15 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups.
- and substituted and unsubstituted heterocyclylamino groups.
- 1 17. The compound of claim 1, wherein \mathbb{R}^7 is an alkoxy group
- 2 having from 1-6 carbon atoms or an alkyl group having from 1-6 carbon atoms.
- 1 18. The compound of claim 1, wherein R⁷ is selected from the
- 2 group consisting of a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴
- 3 where n is an integer selected from 0, 1, or 2 and R¹⁴ is selected from substituted
- 4 and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and
- 5 substituted and unsubstituted heterocyclyl groups.
- 1 19. The compound of claim 1, wherein R^7 is a substituted amino
- 2 group having the formula -N(R¹⁵)CH₂(CH₂)_nR¹⁶ where n is an integer selected from
- 3 0, 1, or 2, R¹⁶ is selected from the group consisting of substituted and unsubstituted
- 4 alkoxy groups, substituted and unsubstituted aryl groups, and substituted and
- 5 unsubstituted heterocyclyl groups, and R¹⁵ is selected from the group consisting of
- 6 -H, and substituted and unsubstituted alkyl groups.
- 1 20. The compound of claim 1, wherein R⁷ is a substituted or
- 2 unsubstituted heterocyclyl group.

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1 21. A compound having the structure I, a tautomer of the

2 compound, a pharmaceutically acceptable salt of the compound, or a

3 pharmaceutically acceptable salt of the tautomer

$$R^{5}$$
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{10}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{10}
 $Z^$

4 I

5 wherein

6 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

7 R¹ is selected from -H, -F, -Cl, -Br, -NO₂, -C \equiv N, -C(=O)-O-alkyl

8 groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and

9 unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl

10 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and

unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl

12 groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and

13 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl

14 groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted

15 -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups,

substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy

17 groups, substituted and unsubstituted amino groups, substituted and unsubstituted

- -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 19 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 20 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 21 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 22 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 23 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 24 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 26 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted
- 27 -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 28 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 29 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 30 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 31 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 32 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 33 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 34 -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 35 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 36 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 37 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- 38 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 39 R^2 is selected from -H, -F, -Cl, -Br, -C=N, -NO₂, -CO₂H, -OH,
- 40 substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino
- 41 groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted
- 42 -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups,
- substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and
- 44 unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 45 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 46 -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl

- groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted
- 49 -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted
- 50 -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 51 -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 52 -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
- 53 -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 54 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 55 groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and
- 56 unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups,
- 57 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 58 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and
- 59 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy,
- 60 substituted and unsubstituted heterocyclylalkoxy groups, substituted and
- 61 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 62 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 63 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 64 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 65 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 67 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 68 -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 69 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
- 70 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 71 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 72 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 73 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 74 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 75 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted
- 76 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted

- 77 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 78 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- 79 -alkyl-N(H)-C(=0)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula
- 80 -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2
- 81 oxygen atoms;
- 82 R³ is selected from -H, -F, -Cl, -Br, -CF₃, -C≡N, substituted and
- 83 unsubstituted alkyl groups, substituted and unsubstituted amino groups, substituted
- and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-O-alkyl
- 85 groups, substituted and unsubstituted arylalkoxy groups, substituted and
- 86 unsubstituted saturated heterocyclyloxy groups, substituted and unsubstituted
- 87 alkoxyalkyl groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted
- and unsubstituted saturated heterocycyl groups, substituted and unsubstituted
- 89 -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl
- 90 groups, substituted and unsubstituted -N(H)-(SO₂)-alkyl groups substituted and
- 91 unsubstituted -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and
- 92 unsubstituted -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted
- 93 -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 95 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 96 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 97 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 98 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 99 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
- 101 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 102 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- 104 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups;

105	R^4 is -H, -F, -Br, -Cl, -NO ₂ , -C=N, -C(=O)-O-alkyl groups, -OH,
106	substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
107	heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups,
108	substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted
109	aryloxy groups, substituted and unsubstituted $-N(H)-C(=O)$ -aryl groups, substituted
110	and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted
111	-N(H)-SO ₂ -alkyl groups, substituted and unsubstituted -N(H)-SO ₂ -aryl groups,
112	-N(H)-SO ₂ -CF ₃ groups, substituted and unsubstituted -N(H)-SO ₂ -heterocyclyl
113	groups, substituted and unsubstituted heterocyclyl groups, substituted and
114	unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted
115	and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl
116	groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups,
117	substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and
118	unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
119	(alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
120	(alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
121	(alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
122	-alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
123	-alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
124	-alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
125	-alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
126	-alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
127	alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
128	substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
129	unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
130	heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
131	-alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
132	-alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
133	-alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted

-alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted and -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;

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R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted amino groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁵ is absent if Z¹ is N;

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups. substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including

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161 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 162 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 163 groups; substituted and unsubstituted heterocyclyl groups including substituted and 164 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 165 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 166 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 167 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups. 168 substituted and unsubstituted amino groups including substituted and unsubstituted 169 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino 170 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 171 unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, 172 173 substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted 174 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 175 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted 176 -C(=O)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N; 177 R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl 178 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 179 amino groups, substituted and unsubstituted alkylamino groups, substituted and 180 unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl 181 groups, or R⁸ is absent if Z⁴ is N; R9 is -H; and 182 R¹⁰ is selected from the group consisting of -H, and substituted and 183 184 unsubstituted alkyl groups, and further wherein at least one of R¹, R², R³, R⁴, R⁵, R⁶, R⁷ or R⁸ is 185 not -H. 186

4 unsubstituted heteroaryloxy group.

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1	22. The compound of claim 21, wherein Z^1 , Z^2 , Z^3 , and Z^4 are C.
1	23. The compound of claim 21, wherein R ¹ is selected from -H,
2	-F, -Cl, or -Br.
1	24. The compound of claim 21, wherein R ² is selected from the
2	group consisting of -H, -F, -Cl, -CO ₂ H, substituted and unsubstituted alkyl groups,
3	substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted
4	-C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
5	substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
6	unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted
7	-N(H)C(=O)-aryl groups, substituted and unsubstituted $-N(H)C(=O)$ -heterocyclyl
8	groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
9	and unsubstituted $-N(H)C(=O)N(H)$ -aryl groups, substituted and unsubstituted
10	-N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups,
11	substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy
12	groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted
13	heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R^2
14	and R³ are a group of formula -OCH2O- such that R² and R³ define a fused
15	5-membered ring that includes 2 oxygen atoms.
	·
1	25. The compound of claim 21, wherein \mathbb{R}^2 is H.
1	26. The compound of claim 21, wherein R ² is an unsubstituted
2	alkoxy group having from 1 to 4 carbon atoms, a substituted or unsubstituted alkyl
3	group, a substituted or unsubstituted arylalkoxy groups, or a substituted or

- 1 27. The compound of claim 21, wherein R³ is selected from the 2 group consisting of -H, -F, -Cl, and -OMe.
- 1 28. The compound of claim 21, wherein R³ is selected from the
- 2 group consisting of -F, -Cl, -Br, -CF₃, -C≡N, substituted and unsubstituted alkyl
- 3 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 4 -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 5 -N(H)C(=O)N(H)-aryl groups and substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula
- 7 -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2
- 8 oxygen atoms.
- 1 29. The compound of claim 21, wherein R⁵ or R⁸ is selected from
- 2 -H, a -CH₃ group, or a morpholine group.
- 1 30. The compound of claim 21, wherein R⁶ is selected from the
- 2 group consisting of -Br, substituted and unsubstituted alkyl groups, substituted and
- 3 unsubstituted alkoxy groups including substituted and unsubstituted
- 4 heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and
- 5 substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 7 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 8 unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted
- 9 -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups
- 10 including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted
- and unsubstituted arylheterocyclyl groups, substituted and unsubstituted
- 12 alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl
- 13 groups; substituted and unsubstituted heterocyclyloxy groups, substituted and
- 14 unsubstituted aryloxy groups, and substituted and unsubstituted amino groups
- 15 including substituted and unsubstituted dialkylamino groups, substituted and

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- 16 unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted
- 17 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups,
- 18 and substituted and unsubstituted heterocyclylamino groups.
- 1 31. The compound of claim 21, wherein R⁶ is an alkoxy group
- 2 having from 1-6 carbon atoms or an alkyl group having from 1-6 carbon atoms.
- 1 32. The compound of claim 21, wherein R⁶ is a substituted alkoxy
- 2 group having the formula -OCH₂(CH₂)_mR¹¹ where m is an integer selected from the
- 3 group consisting of 0, 1, and 2 and R11 is selected from the group consisting of
- 4 substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryl
- 5 groups, and substituted and unsubstituted heterocyclyl groups.
- 1 33. The compound of claim 21, wherein R⁶ is a substituted amino
- 2 group having the formula $-N(R^{12})(CH_2)_pR^{13}$ where p is an integer selected from 0, 1.
- 3 2, or 3, R¹³ is selected from the group consisting of substituted and unsubstituted
- 4 alkoxy groups, substituted and unsubstituted amino groups, substituted and
- 5 unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and
- 6 R¹² is selected from the group consisting of -H, and substituted and unsubstituted
- 7 alkyl groups.
- 1 34. The compound of claim 21, wherein R⁶ is a substituted or
- 2 unsubstituted heterocyclyl group.
- 1 35. The compound of claim 21, wherein at least one of R^6 or R^7 is
- 2 -H.
- 1 36. The compound of claim 21, wherein R^7 is selected from the
- 2 group consisting of substituted and unsubstituted alkyl groups, substituted and
- 3 unsubstituted alkoxy groups including substituted and unsubstituted

- 4 heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and
- 5 substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 7 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 8 unsubstituted -C(=0)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted
- 9 -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups
- 10 including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted
- and unsubstituted arylheterocyclyl groups, substituted and unsubstituted
- 12 alkylheterocyclyl groups and substituted and unsubstituted cycloalkylheterocyclyl
- 13 groups; substituted and unsubstituted heterocyclyloxy groups, substituted and
- 14 unsubstituted aryloxy groups, and substituted and unsubstituted amino groups
- 15 including substituted and unsubstituted dialkylamino groups, substituted and
- 16 unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted
- 17 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups,
- 18 and substituted and unsubstituted heterocyclylamino groups.
- The compound of claim 21, wherein \mathbb{R}^7 is an alkoxy group
- 2 having from 1-6 carbon atoms or an alkyl group having from 1-6 carbon atoms.
- 1 38. The compound of claim 21, wherein R^7 is selected from the
- 2 group consisting of a substituted alkoxy group having the formula -OCH2(CH2)nR14
- 3 where n is an integer selected from 0, 1, or 2 and R¹⁴ is selected from substituted
- 4 and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and
- 5 substituted and unsubstituted heterocyclyl groups.
- The compound of claim 21, wherein \mathbb{R}^7 is a substituted amino
- 2 group having the formula $-N(R^{15})(CH_2)_qR^{16}$ where q is an integer selected from 0, 1,
- 3 2, or 3, R¹⁶ is selected from the group consisting of substituted and unsubstituted
- 4 alkoxy groups, substituted and unsubstituted aryl groups, and substituted and

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5 unsubstituted heterocyclyl groups, and R¹⁵ is selected from the group consisting of

- 6 -H, and substituted and unsubstituted alkyl groups.
- 1 40. The compound of claim 21, wherein \mathbb{R}^7 is a substituted or
- 2 unsubstituted heterocyclyl group.
- 1 41. The compound of claim 21, wherein R³ is selected from -F,
- 2 -Cl, or -OMe.
- 1 42. The compound of claim 21, wherein R² is a substituted or
- 2 unsubstituted amino group selected from the group consisting of substituted and
- 3 unsubstituted alkylamino groups, dialkylamino groups, cycloalkylamino groups,
- 4 heterocyclylamino groups, heterocyclylalkylamino groups, arylalkylamino groups,
- 5 arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups.
- 1 43. The compound of claim 21, wherein R³ is a substituted and
- 2 unsubstituted -C(=O)N(H)-alkyl-heterocyclyl groups where the heterocyclyl group
- 3 of the -C(=O)N(H)-alkyl-heterocyclyl groups is selected from the group consisting
- 4 of morpholinyl, piperazinyl, and piperidinyl groups.
- 1 44. The compound of claim 21, wherein R² is a substituted or
- 2 unsubstituted amino group selected from the group consisting of substituted and
- 3 unsubstituted alkylamino groups, dialkylamino groups, cycloalkylamino groups,
- 4 heterocyclylamino groups, heterocyclylalkylamino groups, arylalkylamino groups,
- 5 arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups.

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1 45. A compound having the structure I, a tautomer of the

2 compound, a pharmaceutically acceptable salt of the compound, or a

3 pharmaceutically acceptable salt of the tautomer

$$R^{5} \qquad Z^{1} \qquad Z^{2} \qquad Z^{3} \qquad R^{7} \qquad R^{8} \qquad R^{10} \qquad R^{10}$$

I

4

5 wherein

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N; 6

7 R^{1} is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl

8 groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and

9 unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl

10 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and

11 unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl

12 groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and

13 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl

14 groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted

-N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, 15

16 substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy

groups, substituted and unsubstituted amino groups, substituted and unsubstituted 17

- 18 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 19 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 20 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 21 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 22 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 23 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 24 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 26 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted
- 27 -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 28 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 29 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 30 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 31 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 32 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 33 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 34 -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 35 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 36 -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 37 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- 38 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 39 R^2 is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH,
- 40 substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino
- 41 groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted
- 42 -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups,
- 43 substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and
- 44 unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted
- -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 46 -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl

- 47 groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and
- 48 unsubstituted -N(H)C(=0)-aryl groups, substituted and unsubstituted
- 49 -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted
- -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 51 -N(H)C(=O)N(H)-arvl groups, substituted and unsubstituted
- 52 -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
- 53 -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 54 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 55 groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and
- 56 unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups,
- 57 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 58 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and
- 59 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy,
- 60 substituted and unsubstituted heterocyclylalkoxy groups, substituted and
- 61 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 62 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 63 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 64 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 65 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 66 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 67 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted
- 68 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 69 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 70 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 71 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 72 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 73 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 74 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 75 -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 76 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted

- 77 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 78 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- 79 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula
- 80 -OCH2O- such that R² and R³ define a fused 5-membered ring that includes 2
- 81 oxygen atoms;
- 82 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H,
- 83 substituted and unsubstituted amino groups, substituted and unsubstituted alkyl
- 84 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 85 -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted
- 86 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl
- 87 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and
- 88 unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups,
- 89 substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and
- 90 unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 91 -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 92 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 93 groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
- and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 95 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 96 -C(=0)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 97 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 98 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 99 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 100 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 101 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted

106 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted 107 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups. 108 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and 109 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted 110 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted 111 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted 112 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted 113 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted 114 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted 115 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; 116 R⁴ is -H, -F, -Br, -Cl, -NO₂, -C≡N, -C(=O)-O-alkyl groups, -OH, 117 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups, 118 119 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted 120 aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted 121 and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and unsubstituted 122 -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, 123 -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl 124 groups, substituted and unsubstituted heterocyclyl groups, substituted and 125 unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted 126 and unsubstituted alkoxy groups, substituted and unsubstituted -C(=0)-N(H)-alkyl 127 groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups. 128 substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and 129 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 130 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 131 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 132 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted 133 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted 134

135 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted 136 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted 137 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, 138 139 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and 140 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted 141 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted 142 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted 143 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted 144 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted 145 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted 146 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; 147 R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl 148 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 149 amino groups, substituted and unsubstituted alkylamino groups, substituted and 150 unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl 151 groups, or R⁵ is absent if Z¹ is N; R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and 152 153 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including 154 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 155 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 156 groups; substituted and unsubstituted heterocyclyl groups including substituted and 157 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 158 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 159 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 160 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, 161 substituted and unsubstituted amino groups including substituted and unsubstituted 162 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino

163 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 164 unsubstituted arylalkylamino groups, and substituted and unsubstituted 165 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, 166 substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted 167 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 168 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or R^6 is absent if Z^2 is N; 169 170 R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and 171 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including 172 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 173 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 174 groups; substituted and unsubstituted heterocyclyl groups including substituted and 175 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 176 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 177 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 178 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, 179 substituted and unsubstituted amino groups including substituted and unsubstituted 180 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino 181 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 182 unsubstituted arylalkylamino groups, and substituted and unsubstituted 183 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, 184 substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted 185 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted 186 -C(=O)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N; 187 R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl 188 189 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 190 amino groups, substituted and unsubstituted alkylamino groups, substituted and

unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

193 R⁹ is -H; and

194 R¹⁰ is selected from the group consisting of -H, and substituted and 195 unsubstituted alkyl groups,

and further wherein at least one of Z² or Z³ is C and at least one of R⁶ 196 197 or R⁷ is selected from the group consisting of -Br, -CO₂H, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy 198 199 groups, substituted and unsubstituted alkoxyalkoxy groups, substituted and 200 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 201 arylheterocyclyl groups, substituted and unsubstituted cycloalkylheterocyclyl 202 groups, substituted and unsubstituted heterocyclyloxy groups, substituted and 203 unsubstituted aryloxy groups, substituted and unsubstituted 204 (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted 205 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, 206 substituted and unsubstituted heterocyclylamino groups, substituted and 207 unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted 208 -C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted 209 210 -C(=O)-heterocyclyl groups.

- 1 46. The compound of claim 45, wherein R³ is selected from the
- 2 group consisting of -F, -Cl, -Br, -CF₃, -C≡N, -NO₂, -CO₂H, substituted and
- 3 unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted
- 4 and unsubstituted alkoxy groups, and substituted and unsubstituted
- 5 -C(=O)N(H)-alkyl-heterocyclyl groups.

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- 1 47. The compound of claim 45, wherein R³ is selected from the
- 2 group consisting of -F, -Cl, -Br, -CF₃, -C≡N, substituted and unsubstituted alkyl
- 3 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 4 -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 5 -N(H)C(=O)N(H)-aryl groups, and substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl-heterocyclyl groups.
- 1 48. The compound of claim 45, wherein R¹ is selected from -H,
- 2 -F, -Cl, or -Br.

1

- 1 49. The compound of claim 45, wherein R² is selected from the
- 2 group consisting of -H, -F, -Cl, -CO₂H, substituted and unsubstituted alkyl groups,
- 3 substituted and unsubstituted -C(=O)O-alkyl groups, substituted and unsubstituted
- 4 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 5 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 6 unsubstituted -N(H)C(=0)-alkyl groups, substituted and unsubstituted
- 7 -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl
- 8 groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
- 9 and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 10 -N(H)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups,
- 11 substituted and unsubstituted alkoxy groups, substituted and unsubstituted arylalkoxy
- 12 groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted
- 13 heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy groups; or R²
- 14 and R³ are a group of formula -OCH₂O- such that R² and R³ define a fused
- 15 5-membered ring that includes 2 oxygen atoms.
 - 50. The compound of claim 45, wherein \mathbb{R}^2 is H.

1 51.	The compound of claim 45,	wherein R ² is an unsubstituted
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- 2 alkoxy group having from 1 to 4 carbon atoms, a substituted or unsubstituted alkyl
- 3 group, a substituted or unsubstituted aryloxy group, or a substituted or unsubstituted
- 4 heteroaryloxy group.
- 1 52. The compound of claim 45, wherein R³ is selected from the
- 2 group consisting of -H, -F, -Cl, and -OMe.
- 1 53. The compound of claim 45, wherein R⁵ or R⁸ is selected from
- 2 -H, a -CH₃ group, or a morpholine group.
- 1 54. The compound of claim 45, wherein R⁶ is selected from the
- 2 group consisting of -Br, substituted and unsubstituted alkyl groups, substituted and
- 3 unsubstituted alkoxy groups including substituted and unsubstituted
- 4 heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and
- 5 substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 7 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 8 unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted
- 9 -C(=O)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups
- 10 including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted
- and unsubstituted arytheterocyclyl groups, substituted and unsubstituted
- 12 alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl
- 13 groups; substituted and unsubstituted heterocyclyloxy groups, substituted and
- 14 unsubstituted aryloxy groups, and substituted and unsubstituted amino groups
- 15 including substituted and unsubstituted dialkylamino groups, substituted and
- 16 unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted
- 17 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups,
- 18 and substituted and unsubstituted heterocyclylamino groups.

1		The compound of claim 45, wherein R ⁶ is an alkoxy group
2	naving from 1-6 carbo	on atoms or an alkyl group having from 1-6 carbon atoms.
1	56.	The compound of claim 45, wherein R ⁶ is a substituted alkoxy
2	group having the form	nula -OCH2(CH2)mR ¹¹ where m is an integer selected from the
3	group consisting of 0,	1, and 2 and R ¹¹ is selected from the group consisting of
4	substituted and unsubs	tituted alkoxy groups, substituted and unsubstituted aryl

- The compound of claim 45, wherein R⁶ is a substituted amino
- 2 group having the formula $-N(R^{12})(CH_2)_pR^{13}$ where p is an integer selected from 0, 1,
- 3 2, or 3, R¹³ is selected from the group consisting of substituted and unsubstituted
- 4 alkoxy groups, substituted and unsubstituted amino groups, substituted and

groups, and substituted and unsubstituted heterocyclyl groups.

- 5 unsubstituted aryl groups, and substituted and unsubstituted heterocyclyl groups, and
- 6 R¹² is selected from the group consisting of -H, and substituted and unsubstituted
- 7 alkyl groups.
- The compound of claim 45, wherein R⁶ is a substituted or unsubstituted heterocyclyl group.
- 1 59. The compound of claim 45, wherein at least one of R⁶ or R⁷ is
- 2 -H.
- 1 60. The compound of claim 45, wherein R^7 is selected from the
- 2 group consisting of substituted and unsubstituted alkyl groups, substituted and
- 3 unsubstituted alkoxy groups including substituted and unsubstituted
- 4 heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and
- 5 substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted
- 6 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,

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- 7 substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and
- 8 unsubstituted -C(=0)N(alkyl)(heterocyclyl) groups, substituted and unsubstituted
- 9 -C(=0)-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups
- 10 including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted
- 11 and unsubstituted arylheterocyclyl groups, substituted and unsubstituted
- 12 alkylheterocyclyl groups and substituted and unsubstituted cycloalkylheterocyclyl
- 13 groups; substituted and unsubstituted heterocyclyloxy groups, substituted and
- 14 unsubstituted aryloxy groups, and substituted and unsubstituted amino groups
- 15 including substituted and unsubstituted dialkylamino groups, substituted and
- 16 unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted
- 17 heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups,
- 18 and substituted and unsubstituted heterocyclylamino groups.
- 1 61. The compound of claim 45, wherein R⁷ is an alkoxy group
- 2 having from 1-6 carbon atoms or an alkyl group having from 1-6 carbon atoms.
- 1 62. The compound of claim 45, wherein R^7 is selected from the
- 2 group consisting of a substituted alkoxy group having the formula -OCH₂(CH₂)_nR¹⁴
- 3 where n is an integer selected from 0, 1, or 2 and R¹⁴ is selected from substituted
- 4 and unsubstituted alkoxy groups, substituted and unsubstituted aryl groups, and
- 5 substituted and unsubstituted heterocyclyl groups.
- 1 63. The compound of claim 45, wherein R⁷ is a substituted amino
- 2 group having the formula $-N(R^{15})(CH_2)_qR^{16}$ where q is an integer selected from 0, 1,
- 3 2, or 3, R¹⁶ is selected from the group consisting of substituted and unsubstituted
- 4 alkoxy groups, substituted and unsubstituted aryl groups, and substituted and
- 5 unsubstituted heterocyclyl groups, and R¹⁵ is selected from the group consisting of
- 6 -H, and substituted and unsubstituted alkyl groups.

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- 1 64. The compound of claim 45, wherein R⁷ is a substituted or 2 unsubstituted heterocyclyl group.
- 1 65. The compound of claim 45, wherein R³ is selected from -F, 2 -Cl, or -OMe.
- 1 66. The compound of claim 45, wherein R² is a substituted or
- 2 unsubstituted amino group selected from the group consisting of substituted and
- 3 unsubstituted alkylamino groups, dialkylamino groups, heterocyclylamino,
- 4 heterocyclylalkylamino groups, heterocyclylamino groups, arylalkylamino groups,
- 5 arylalkoxyarylmethylamino groups, and aryloxyarylalkylamino groups.
- 1 67. The compound of claim 45, wherein R³ is a substituted and
- 2 unsubstituted -C(=0)N(H)-alkyl-heterocyclyl groups where the heterocyclyl group
- 3 of the -C(=O)N(H)-alkyl-heterocyclyl groups is selected from the group consisting
- 4 of morpholinyl, piperazinyl, and piperidinyl groups.

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1 68. A compound having the structure I, a tautomer of the

2 compound, a pharmaceutically acceptable salt of the compound, or a

3 pharmaceutically acceptable salt of the tautomer

$$R^{5} \qquad Z^{1} \qquad Z^{2} \qquad Z^{3} \qquad R^{7} \qquad Z^{4} \qquad R^{8} \qquad R^{10} \qquad$$

I 4

5 wherein

 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N; 6

7 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl

8 groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and

9 unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl

groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and 10

11 unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl

groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 12

unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl 13

groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted 14

-N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, 15

substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 16

groups, substituted and unsubstituted amino groups, substituted and unsubstituted 17

- -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 19 -C(=0)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 20 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 21 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 22 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 23 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 24 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 25 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
- 26 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted
- 27 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 28 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
- 29 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 30 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 31 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 32 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 33 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted
- 36 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 37 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- -aikyl-N(H)-C(=O)-aikyl-heterocyclyl groups;
- 39 R^2 is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH,
- 40 substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino
- 41 groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted
- 42 -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups,
- 43 substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and
- 44 unsubstituted -C(=0)N(H)-alkyl groups, substituted and unsubstituted
- 45 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 46 -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl

- 47 groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and
- 48 unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted
- 49 -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted
- -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 51 N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 52. -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
- -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 54 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 55 groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and
- 56 unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups,
- 57 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 58 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and
- 59 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy,
- 60 substituted and unsubstituted heterocyclylalkoxy groups, substituted and
- 61 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 62 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 63 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 64 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 65 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 66 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 67 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 68 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 69 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 70 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 71 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 72 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 73 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 74 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 75 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted
- 76 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted

- 77 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 78 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- 79 -alkyl-N(H)-C(=0)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula
- 80 -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2
- 81 oxygen atoms;
- 82 R³ is selected from -F, -Cl, -Br, -CF₃, -C≡N, substituted and
- 83 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted
- 84 and unsubstituted arylalkoxy groups, substituted and unsubstituted saturated
- 85 heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups,
- 86 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted
- 87 saturated heterocycyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl
- 88 groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and
- 89 unsubstituted -N(H)-(SO₂)-alkyl groups substituted and unsubstituted
- 90 -N(H)-(SO₂)-aryl groups, -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted
- 91 -N(H)-(SO₂)-heterocyclyl groups, substituted and unsubstituted
- 92 -N(H)C(=O)N(H)-alkyl groups, and substituted and unsubstituted
- 93 -N(H)C(=O)N(H)-aryl;
- 94 R^4 is -H, -F, -Br, -Cl, -NO₂, -C \equiv N, -C(\equiv O)-O-alkyl groups, -OH,
- 95 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 96 heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups,
- 97 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted
- 98 aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted
- 99 and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and unsubstituted
- 100 -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups,
- 101 -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl
- 102 groups, substituted and unsubstituted heterocyclyl groups, substituted and
- 103 unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted
- and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl

105	groups, substituted and unsubstituted $-C(=O)-N(H)$ -alkyl-heterocyclyl groups,
106	substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and
107	unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
108	(alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
109	(alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
110	(alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
111	-alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
112	-alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
113	-alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
114	-alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
115	-alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
116	alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
117	substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
118	unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
119	heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
120	-alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
121	-alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
122	-alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
123	-alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
124	-alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
125	R ⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl
126	groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
127	amino groups, substituted and unsubstituted alkylamino groups, substituted and
128	unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl
129	groups, or R ⁵ is absent if Z ¹ is N;
130	R ⁶ is selected from -H, -F, -Cl, -Br, -CF ₃ , -CO ₂ H, substituted and
131	unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including
	amanana ami, b. oaks, sasanasa amananasa amani, b. saks maranas

substituted and unsubstituted heterocyclylalkoxy groups, substituted and

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unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups. substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=0)N(H)-heterocyclyl groups, substituted and unsubstituted -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R^6 is absent if Z^2 is N;

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted and u

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162	substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted
163	-C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
164	-C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted
165	-C(=0)-heterocyclyl groups; or R^7 is absent if Z^3 is N;
166	R ⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl
167	groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
168	amino groups, substituted and unsubstituted alkylamino groups, substituted and
169	unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl
170	groups, or R^8 is absent if Z^4 is N;
171	R ⁹ is -H; and
172	R ¹⁰ is selected from the group consisting of -H, and substituted and

173 unsubstituted alkyl groups.

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1 69. A compound having the structure I, a tautomer of the

- 2 compound, a pharmaceutically acceptable salt of the compound, or a
- 3 pharmaceutically acceptable salt of the tautomer

$$R^{5}$$
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{4}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{10}

I

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5 wherein

Z¹, Z², Z³, and Z⁴ are independently selected from C or N; 6

7 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C=N, -C(=0)-O-alkyl

8 groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and

- 9 unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl
- 10 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and
- unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl 11
- 12 groups, substituted and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and
- 13 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl
- 14 groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted
- 15 -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups,
- substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 16
- 17 groups, substituted and unsubstituted amino groups, substituted and unsubstituted

- 18 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 19 -C(=0)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 20 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 21 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 22 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 23 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 24 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 26 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 27 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 28 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 29 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 30 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 31 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 32 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 33 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 34 -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 35 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 36 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 37 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 39 R² is selected from -F, -Cl, -Br, -C≡N, -CO₂H, -OH, substituted and
- 40 unsubstituted guanidinyl groups, substituted and unsubstituted -C(=O)O-alkyl
- 41 groups, substituted and unsubstituted -C(=0)O-aryl groups, substituted and
- 42 unsubstituted -C(=0)O-heteroaryl groups, substituted and unsubstituted
- 43 -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups,
- 44 substituted and unsubstituted -C(=0)N(H)-heterocyclyl groups, substituted and
- unsubstituted -N(H)C(=O)-alkyl groups, substituted and unsubstituted
- 46 -N(H)C(=O)-aryl groups, substituted and unsubstituted -N(H)C(=O)-heterocyclyl

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- groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted 47
- and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted 48
- 49 -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
- -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups, 50
- -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl 51
- 52 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 53 arylalkoxy groups, substituted and unsubstituted aryloxy groups, substituted and
- 54 unsubstituted heterocyclyloxy, and substituted and unsubstituted heterocyclylalkoxy
- groups; or R² and R³ are a group of formula -OCH₂O- such that R² and R³ define a 55
- 56 fused 5-membered ring that includes 2 oxygen atoms;
- 57 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H,
- 58 substituted and unsubstituted amino groups, substituted and unsubstituted alkyl
- 59 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 60 -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted
- 61 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl
- 62 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and
- 63 unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups,
- 64 substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and
- 65 unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 66 -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 67 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 68 groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
- 69 and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 70 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 71 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 72 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 73 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 74 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 75 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted

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76 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted

- 77 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 78 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted
- 79 -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 80 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 82 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 83 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 84 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 85 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 86 -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 87 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 88 -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 89 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- 90 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 91 R^4 is -H, -F, -Br, -Cl, -NO₂, -C=N, -C(=O)-O-alkyl groups, -OH,
- 92 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 93 heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups,
- 94 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted
- 95 aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted
- and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 97 -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups,
- 98 -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl
- 99 groups, substituted and unsubstituted heterocyclyl groups, substituted and
- 100 unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted
- and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl
- groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups,
- substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and
- unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted

105 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 106 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 107 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 108 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted 109 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted 110 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted 111 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted 112 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted 113 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, 114 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted 115 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted 116 117 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted 118 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted 119 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted 120 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted 121 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups; R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl 122 123 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 124 amino groups, substituted and unsubstituted alkylamino groups, substituted and 125 unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl 126 groups, or R⁵ is absent if Z¹ is N; 127 R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including 128 129 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 130 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 131 groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 132

133 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 134 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 135 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, 136 substituted and unsubstituted amino groups including substituted and unsubstituted 137 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino 138 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 139 unsubstituted arylalkylamino groups, and substituted and unsubstituted 140 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted 141 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 142 143 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or \mathbb{R}^6 is absent if \mathbb{Z}^2 is N; 144

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R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted amino groups including substituted and unsubstituted dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and unsubstituted arylalkylamino groups, and substituted and unsubstituted heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted

161 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted

162 -C(=0)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N;

R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted among groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl groups, or R⁸ is absent if Z⁴ is N;

 R^9 is -H; and

169 R¹⁰ is selected from the group consisting of -H, and substituted and 170 unsubstituted alkyl groups.

1 70. A compound having the structure I, a tautomer of the

2 compound, a pharmaceutically acceptable salt of the compound, or a

3 pharmaceutically acceptable salt of the tautomer

$$R^5$$
 Z^1
 Z^2
 Z^3
 Z^4
 Z^4

I

5 wherein

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 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

7 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C \equiv N, -C(=0)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and 8 9 unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl 10 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and 11 unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 12 13 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl 14 groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, 15 substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 16 17 groups, substituted and unsubstituted amino groups, substituted and unsubstituted 18 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted 19 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted 20 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted 21 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 22 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 23 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 24 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted 26 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted 27 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted 28 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted 29 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted 30 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, 31 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and 32 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted 33 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted

-alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted

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- 35 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 36 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 37 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- R² is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH,
- 40 substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino
- 41 groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted
- 42 -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups,
- 43 substituted and unsubstituted -C(=O)O-heteroaryl groups, substituted and
- 44 unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 45 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 46 -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl
- 47 groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and
- 48 unsubstituted -N(H)C(=0)-aryl groups, substituted and unsubstituted
- 49 -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted
- 50 -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 52 -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
- 53 -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 54 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 55 groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and
- 56 unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups,
- 57 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 58 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and
- 59 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy,
- 60 substituted and unsubstituted heterocyclylalkoxy groups, substituted and
- 61 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 62 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 63 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted

- 64 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 65 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 66 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 67 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 68 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 69 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 70 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 71 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 72 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 73 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 74 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 75 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted
- 76 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted
- 77 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 78 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- 79 -alkyl-N(H)-C(=0)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula
- 80 -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2
- 81 oxygen atoms;
- 82 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C=N, -NO₂, -CO₂H,
- 83 substituted and unsubstituted amino groups, substituted and unsubstituted alkyl
- 84 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 85 -C(=0)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted
- 86 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl
- 87 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and
- 88 unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups,
- 89 substituted and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and
- 90 unsubstituted -N(H)-C(=0)-aryl groups, substituted and unsubstituted
- 91 -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 92 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl

- 93 groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
- 94 and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 95 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-
- 96 heterocyclyl groups, substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups,
- 97 substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and
- 98 unsubstituted (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 99 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 100 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 101 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 102 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 103 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 104 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
- 105 -alkyl-N(alkyl)-C(=0)-alkyl-heterocyclyl groups, substituted and unsubstituted
- alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 107 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 108 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 109 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 110 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 112 -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 115 R^4 is -H, -F, -Br, -Cl, -NO₂, -C \equiv N, -C(\equiv O)-O-alkyl groups, -OH,
- 116 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 117 heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups,
- 118 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted
- 119 aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted
- 120 and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 121 -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups,

122	-N(H)-SO ₂ -CF ₃ groups, substituted and unsubstituted -N(H)-SO ₂ -heterocyclyl
123	groups, substituted and unsubstituted heterocyclyl groups, substituted and
124	unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted
125	and unsubstituted alkoxy groups, substituted and unsubstituted $-C(=O)-N(H)$ -alkyl
126	groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups,
127	substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and
128	unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
129	(alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
130	(alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
131	(alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
132	-alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
133	-alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
134	-alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
135	-alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
136	-alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
137	alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
138	substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
139	unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
140	heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
141	-alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
142	-alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted
143	-alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
144	-alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
145	-alkyl-N(H)-C(=0)-alkyl-heterocyclyl groups;
146	R ⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl
147	groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
148	amino groups, substituted and unsubstituted alkylamino groups, substituted and
149	unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl

150 groups, or R⁵ is absent if Z¹ is N;

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R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and 151 152 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including 153 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 154 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 155 groups; substituted and unsubstituted heterocyclyl groups including substituted and 156 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 157 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 158 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 159 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups. 160 substituted and unsubstituted amino groups including substituted and unsubstituted 161 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino 162 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 163 unsubstituted arylalkylamino groups, and substituted and unsubstituted 164 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, 165 substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted 166 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 167 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or R^6 is absent if Z^2 is N; 168 169 R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and 170 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including 171 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 172 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 173 groups; substituted and unsubstituted heterocyclyl groups including substituted and 174 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 175 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 176 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups, 177 substituted and unsubstituted amino groups including substituted and unsubstituted 178 179 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino

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180 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 181 unsubstituted arylalkylamino groups, and substituted and unsubstituted 182 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, 183 substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted 184 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 185 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=O)-heterocyclyl groups; or R^7 is absent if Z^3 is N; 186 R⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl 187 188 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted 189 amino groups, substituted and unsubstituted alkylamino groups, substituted and 190 unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl 191 groups, or R⁸ is absent if Z⁴ is N; R⁹ is -H; and 192 R¹⁰ is selected from the group consisting of -H, and substituted and 193 194 unsubstituted alkyl groups, 195 and further wherein at least one of Z² or Z³ is C and at least one of R⁶ or R⁷ is selected from the group consisting of substituted and unsubstituted 196 197 piperidinyl substituted heterocyclyl groups, substituted and unsubstituted 198 heterocyclyl substituted piperidinyl groups, substituted and unsubstituted 199 hydroxymethyl substituted piperidinyl groups, dimethylaminoalkyl substituted 200 pyrrolidinyl groups, substituted and unsubstituted 3-alkyl substituted piperazinyl 201 groups, substituted and unsubstituted 3,5-dialkyl substituted piperazinyl groups, 202 substituted and unsubstituted N-hydroxyalkyl substituted piperazinyl groups, 203 substituted and unsubstituted 1,4-diazacycloheptyl groups, substituted and unsubstituted 1-aza-4-oxacycloheptane groups, substituted and unsubstituted N-204

ethylpiperazinyl groups, substituted and unsubstituted N-isopropylpiperazinyl

205

200	groups, substituted and unsubstituted in-sec-butylpiperazinyi groups, substituted and
207	unsubstituted N-2-pyridyl substituted piperazinyl groups, substituted and
208	unsubstituted N-3-pyridyl substituted piperazinyl groups, substituted and
209	unsubstituted N-4-pyridyl substituted piperazinyl groups, substituted and
210	unsubstituted N(H)-CH2-pyridyl groups, substituted and unsubstituted imidazolyl
211	groups, substituted and unsubstituted 3-alkyl substituted morpholinyl groups,
212	substituted and unsubstituted 3,5-dialkyl substituted morpholinyl groups,
213	dialkylamino substituted pyrrolidinyl groups, pyrrolidinyl groups substituted with
214	both dialkylamino and alkyl groups, substituted and unsubstituted 4-hydroxy
215	substituted piperidinyl groups, substituted and unsubstituted 4-aryl substituted
216	piperidinyl groups, substituted and unsubstituted 4-hydroxy-4-phenyl substituted
217	piperidinyl groups, substituted and unsubstituted cyclohexylpiperazinyl groups,
218	substituted and unsubstituted cyclopentylpiperazinyl groups, substituted and
219	unsubstituted N-alkyl substituted diazabicycloalkane groups, substituted and
220	unsubstituted -N(CH3)(N-alkyl(4-piperidinyl)) groups, substituted and unsubstituted
221	piperazinyl groups further substituted with a -C(=O)-alkyl group bonded to one of
222	the N atoms of the piperazinyl group, substituted and unsubstituted
223	-N(H)CH2CH2-imidazolyl groups, substituted and unsubstituted
224	-N(H)CH2CH2-pyrrolidinyl groups, substituted and unsubstituted
225	-N(H)CH2CH2CH2-morpholinyl groups, substituted and unsubstituted
226	-N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted
227	-N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted
228	-N(H)CH2CH2CH2-pyridyl groups, substituted and unsubstituted
229	-N(H)CH2CH2-imidazolyl groups, substituted and unsubstituted
230	-N(H)CH2CH2-pyrrolidinyl groups, substituted and unsubstituted
231	-N(H)CH2CH2-morpholinyl groups, substituted and unsubstituted
232	-N(H)CH2CH2-piperazinyl groups, substituted and unsubstituted
233	-N(H)CH2CH2-piperidinyl groups, substituted and unsubstituted
234	$-N(H)CH_2CH_2-pyridyl\ groups,\ substituted\ and\ unsubstituted\ \ cyclobutylpiperazinyl$
235	groups, substituted and unsubstituted -OCH2-pyrrolidinyl groups, substituted and

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236 unsubstituted -OCH2CH2-pyrrolidinyl groups, substituted and unsubstituted 237 -OCH₂CH₂CH₂-pyrrolidinyl groups, substituted and unsubstituted piperazinyl groups 238 further substituted with a -CH₂C(=0)-O-alkyl group bonded to one of the N atoms 239 of the piperazinyl group, substituted and unsubstituted piperazinyl groups further 240 substituted with a -C(=0)-O-alkyl group bonded to one of the N atoms of the piperazinyl group, substituted and unsubstituted hydroxypyrrolidinyl groups, 241 242 substituted and unsubstituted hydroxypiperidinyl groups, substituted and 243 unsubstituted -OCH2-pyridyl groups, substituted and unsubstituted piperidinylamino 244 groups, substituted and unsubstituted pyridyloxy groups with a -C(=O)-N(H)(alkyl)245 group bonded to a carbon atom of the pyridine ring of the pyridyloxy group, and 246 substituted and unsubstituted pyridyloxy groups with a -C(=0)-N(alkyl)2 group 247 bonded to a carbon atom of the pyridine ring of the pyridyloxy group.

71. A compound having the structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a

3 pharmaceutically acceptable salt of the tautomer

$$R^{5}$$
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{1}
 Z^{4}
 Z^{4}
 Z^{8}
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{4}
 Z^{4}
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 Z^{8}
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{8}
 Z^{1}
 Z^{2}
 Z^{3}
 Z^{4}
 Z^{4}
 Z^{4}
 Z^{4

I

5 wherein

1

2

4

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 Z^1 , Z^2 , Z^3 , and Z^4 are independently selected from C or N;

7 R^1 is selected from -H, -F, -Cl, -Br, -NO₂, -C \equiv N, -C(\equiv O)-O-alkyl groups, -OH, substituted and unsubstituted arylalkoxy groups, substituted and 8 unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl 9 10 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl 11 12 groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and 13 unsubstituted -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups, -N(H)-SO₂-CF₃ groups, substituted and unsubstituted 14 15 -N(H)-SO₂-heterocyclyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy 16 17 groups, substituted and unsubstituted amino groups, substituted and unsubstituted 18 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted 19 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted 20 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted 21 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted 22 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted 23 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted 24 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted 25 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted 26 -alkyl-N(alkyl)-C(=0)-aryl groups, substituted and unsubstituted -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted 27 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted 28 29 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted 30 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, 31 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and 32 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted 33 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted

-alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted

34

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- 35 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted
- 36 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 37 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- 38 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- R² is selected from -H, -F, -Cl, -Br, -C \equiv N, -NO₂, -CO₂H, -OH,
- 40 substituted and unsubstituted guanidinyl groups, substituted and unsubstituted amino
- 41 groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted
- 42 -C(=O)O-alkyl groups, substituted and unsubstituted -C(=O)O-aryl groups,
- 43 substituted and unsubstituted -C(=0)O-heteroaryl groups, substituted and
- 44 unsubstituted -C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 45 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 46 -C(=O)N(H)-aryl groups, substituted and unsubstituted -C(=O)N(H)-heterocyclyl
- 47 groups, substituted and unsubstituted -N(H)C(=O)-alkyl groups, substituted and
- 48 unsubstituted -N(H)C(=O)-aryl groups, substituted and unsubstituted
- 49 -N(H)C(=O)-heterocyclyl groups, substituted and unsubstituted
- -N(H)C(=O)N(H)-alkyl groups, substituted and unsubstituted
- 51 N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 52 -N(H)C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
- 53 -N(H)-(SO₂)-alkyl groups, substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 54 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl
- 55 groups, substituted and unsubstituted -N(H)-heterocyclyl groups, substituted and
- 56 unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups,
- 57 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 58 aryloxy groups, substituted and unsubstituted akoxyalkyl groups, substituted and
- 59 unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted heterocyclyloxy,
- 60 substituted and unsubstituted heterocyclylalkoxy groups, substituted and
- 61 unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 62 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 63 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted

- 64 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 65 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 66 -alkyl-N(alkyl)-C(=0)-alkyl groups, substituted and unsubstituted
- 67 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 68 -alkyl-N(alkyl)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 69 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
- 70 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 71 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 72 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 73 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 74 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- 75 -alkyl-N(H)-C(=0)-alkyl groups, substituted and unsubstituted
- 76 -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted
- 77 -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- 78 -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- 79 -alkyl-N(H)-C(=0)-alkyl-heterocyclyl groups; or R² and R³ are a group of formula
- 80 -OCH₂O- such that R² and R³ define a fused 5-membered ring that includes 2
- 81 oxygen atoms;
- 82 R^3 is selected from -H, -F, -Cl, -Br, -CF₃, -C \equiv N, -NO₂, -CO₂H,
- 83 substituted and unsubstituted amino groups, substituted and unsubstituted alkyl
- 84 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 85 -C(=O)-O-alkyl groups, substituted and unsubstituted arylalkoxy groups, substituted
- 86 and unsubstituted heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl
- 87 groups, substituted and unsubstituted arylalkoxyalkyl groups, substituted and
- 88 unsubstituted aryloxy group, substituted and unsubstituted heterocycyl groups,
- 89 substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and
- 90 unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted
- 91 -N(H)-(SO₂)-alkyl groups substituted and unsubstituted -N(H)-(SO₂)-aryl groups,
- 92 -N(H)-(SO₂)-CF₃ groups, substituted and unsubstituted -N(H)-(SO₂)-heterocyclyl

- 93 groups, substituted and unsubstituted -N(H)C(=O)N(H)-alkyl groups, substituted
- 94 and unsubstituted -N(H)C(=O)N(H)-aryl groups, substituted and unsubstituted
- 95 -C(=O)-N(H)-alkyl groups, substituted and unsubstituted
- 96 -C(=O)-N(H)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 97 (alkyl)(alkyl)aminoalkyl groups, substituted and unsubstituted
- 98 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 99 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 100 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 101 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 102 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
- 103 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 104 -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 105 -alkyl-N(alkyl)-C(=0)-alkyl-aryl groups, substituted and unsubstituted
- 106 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 108 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 109 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 110 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=0)-aryl groups, substituted and unsubstituted
- 113 -alkyl-N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 114 -alkyl-N(H)-C(=O)-alkyl-aryl groups, and substituted and unsubstituted
- 115 -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 116 R^4 is -H, -F, -Br, -Cl, -NO₂, -C \equiv N, -C(\equiv O)-O-alkyl groups, -OH,
- 117 substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted
- 118 heterocyclyloxy groups, substituted and unsubstituted alkoxyalkyl groups,
- 119 substituted and unsubstituted arylalkoxyalkyl groups, substituted and unsubstituted
- 120 aryloxy groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted
- and unsubstituted -N(H)-C(=0)-alkyl groups, substituted and unsubstituted

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- 122 -N(H)-SO₂-alkyl groups, substituted and unsubstituted -N(H)-SO₂-aryl groups,
- 123 -N(H)-SO₂-CF₃ groups, substituted and unsubstituted -N(H)-SO₂-heterocyclyl
- 124 groups, substituted and unsubstituted heterocyclyl groups, substituted and
- 125 unsubstituted amino groups, substituted and unsubstituted alkyl groups, substituted
- 126 and unsubstituted alkoxy groups, substituted and unsubstituted -C(=O)-N(H)-alkyl
- groups, substituted and unsubstituted -C(=O)-N(H)-alkyl-heterocyclyl groups,
- 128 substituted and unsubstituted (alkyl)(alkyl)aminoalkyl groups, substituted and
- 129 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted
- 130 (alkyl)(heterocyclyl)aminoalkyl groups substituted and unsubstituted
- 131 (alkyl)(arylalkyl)aminoalkyl groups, substituted and unsubstituted
- 132 (alkyl)(heterocyclylalkyl)aminoalkyl groups, substituted and unsubstituted
- 133 -alkyl-N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
- 134 -alkyl-N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
- 135 -alkyl-N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted
- 136 -alkyl-N(alkyl)-C(=O)-alkyl-aryl groups, substituted and unsubstituted
- 137 -alkyl-N(alkyl)-C(=O)-alkyl-heterocyclyl groups, substituted and unsubstituted
- 138 alkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups,
- 139 substituted and unsubstituted heterocyclylaminoalkyl groups substituted and
- 140 unsubstituted arylalkylaminoalkyl groups, substituted and unsubstituted
- 141 heterocyclylalkylaminoalkyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
- 143 -alkyl-N(H)-C(=O)-aryl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=0)-heterocyclyl groups, substituted and unsubstituted
- -alkyl-N(H)-C(=0)-alkyl-aryl groups, and substituted and unsubstituted
- -alkyl-N(H)-C(=O)-alkyl-heterocyclyl groups;
- 147 R⁵ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl
- 148 groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
- 149 amino groups, substituted and unsubstituted alkylamino groups, substituted and

unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl

151 groups, or R⁵ is absent if Z¹ is N;

170

171

172

173

174

175

176

177

R⁶ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and 152 153 unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including 154 substituted and unsubstituted heterocyclylalkoxy groups, substituted and 155 unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy 156 groups; substituted and unsubstituted heterocyclyl groups including substituted and 157 unsubstituted heterocyclylheterocyclyl groups, substituted and unsubstituted 158 arylheterocyclyl groups, substituted and unsubstituted alkylheterocyclyl groups, and 159 substituted and unsubstituted cycloalkylheterocyclyl groups; substituted and 160 unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups. 161 substituted and unsubstituted amino groups including substituted and unsubstituted 162 dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino 163 groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and 164 unsubstituted arylalkylamino groups, and substituted and unsubstituted 165 heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups, 166 substituted and unsubstituted -C(=0)N(H)-aryl groups, substituted and unsubstituted 167 -C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted 168 -C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted -C(=0)-heterocyclyl groups; or R^6 is absent if Z^2 is N; 169

R⁷ is selected from -H, -F, -Cl, -Br, -CF₃, -CO₂H, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkoxy groups including substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted arylalkoxy groups, and substituted and unsubstituted alkoxyalkoxy groups; substituted and unsubstituted heterocyclyl groups including substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted arylheterocyclyl groups, substituted alkylheterocyclyl groups, and substituted and unsubstituted and unsubstitute

178	unsubstituted heterocyclyloxy groups, substituted and unsubstituted aryloxy groups,
179	substituted and unsubstituted amino groups including substituted and unsubstituted
180	dialkylamino groups, substituted and unsubstituted (alkyl)(heterocyclyl)amino
181	groups, substituted and unsubstituted heterocyclylalkylamino groups, substituted and
182	unsubstituted arylalkylamino groups, and substituted and unsubstituted
183	heterocyclylamino groups; substituted and unsubstituted -C(=O)N(H)-alkyl groups,
184	substituted and unsubstituted -C(=O)N(H)-aryl groups, substituted and unsubstituted
185	-C(=O)N(H)-heterocyclyl groups, substituted and unsubstituted
186	-C(=O)N(alkyl)(heterocyclyl) groups, and substituted and unsubstituted
187	-C(=O)-heterocyclyl groups; or \mathbb{R}^7 is absent if \mathbb{Z}^3 is N;
188	R ⁸ is selected from -H, -F, -Cl, substituted and unsubstituted alkyl
189	groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted
190	amino groups, substituted and unsubstituted alkylamino groups, substituted and
191	unsubstituted dialkylamino groups, and substituted and unsubstituted heterocyclyl
192	groups, or R ⁸ is absent if Z ⁴ is N;
193	R ⁹ is -H; and
194	R ¹⁰ is selected from the group consisting of -H, and substituted and
195	unsubstituted alkyl groups,
196	and further wherein at least one of the following is true:
	.
197	(i) R ¹ is selected from the group consisting of unsubstituted -NH ₂
198	groups, and substituted and unsubstituted pyrrolidinylalkylamino groups;
•	gerage, and course and conserve pyrronamy amy amino Broups,
199	(ii) R ² is selected from the group consisting of substituted and
	unsubstituted this rolvalkylaming groups substituted and unsubstituted

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201	pyrrolidinylalkylamino groups, and substituted and unsubstituted aminoalkylamino
202	groups; or
203	(iii) R ³ is selected from the group consisting of substituted and
204	unsubstituted thiazolylalkylamino groups, substituted and unsubstituted
205	benzimidazolylalkylamino groups, substituted and unsubstituted
206	imidazolylalkylamino groups, substituted and unsubstituted furanylalkylamino
207	groups, and substituted and unsubstituted arylalkylamino groups.

INTERNATIONAL SEARCH REPORT

onal Application No PCT/US 02/20844

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D403/04 C07D471/04 C07D487/08 C07D473/00 C07D401/14 A61P5/50 C07D403/14 C07D491/04 A61K31/4184 A61P25/00 A61P25/16 A61P37/02 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) CO7D A61K A61P IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. WO 01 53268 A (AGOURON PHARMA) 21 P,X 26 July 2001 (2001-07-26) cited in the application Abstract; page 1, lines 9-15; claims 1,13,22. WO 01 02369 A (AGOURON PHARMA) X 1-71 11 January 2001 (2001-01-11) cited in the application Abstract; claim 1; claim 12, first formula; e.g. examples 42(b), 53(a)-(g), Patent family members are listed in annex. Further documents are listed in the continuation of box C. X Special categories of cited documents: *T° later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the *A* document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled O document referring to an oral disclosure, use, exhibition or document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 14 November 2002 21/11/2002 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016 Weisbrod, T

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